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TITLE: Quality of Life and Functional Status Across the Life  
Courses (Behavioral Center of Excellence Award)

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<b>13. ABSTRACT (Maximum 200 Words)</b>  This Behavioral Center of Excellence in Breast Cancer contains three separate, but related research projects focused on breast cancer patients' quality of life and functional status. There is also a Biostatistic's Core Facility supporting all three studies. The three projects are: <u>Project 1</u> ) Menstrual Cycle Maintenance and Quality of Life Following Treatment for Breast Cancer: A Prospective Study. This is a study of women aged 45 years and younger diagnosed with a first breast cancer. <u>Project 2</u> ) Investigating Mechanisms to Explain Age Associated Differences in Quality of Life Among Breast Cancer Patients. This study examines psychosocial and clinical factors associated with patient's (aged 18-80+ years) coping and quality of life during the first 18 months post-diagnosis. <u>Project 3</u> ) Research on Optimal Recovery Practices in Breast Cancer (RESTORE). This is a randomized exercise intervention trial with a lymphedema prevention program. Project 1 is a continuation of a study that was initiated in January of 1998. Projects 2 and 3 are new protocols, which will begin patient recruitment in the fall of 2002. All three studies have the potential to greatly improve the functional status and life quality of breast cancer patients during treatment and beyond.				
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## OVERVIEW OF CENTER ACTIVITIES

### I. Progress of the Center-Specific Projects and Biostatistic's Core Facility

Summaries of the activities and progress of the 3 research projects and the Biostatistic's Core Facility are included in the annual reports for each specific project and Core. (See Table of Contents.)

### II. Post-Doctoral Fellows

Currently, this Center Grant supports 2 post-doctoral fellows: Dr. Stephanie Walsh and Dr. Deborah Farmer. These fellows have participated in a variety of training and professional activities described below.

Recruitment for one additional (and final) post-doctoral fellow is underway currently. Ads have been placed in the *American Journal of Public Health*, the *APA (American Psychological Association) Monitor*, and *Outlook* – Publication of the Society of Behavioral Medicine (website only). Electronic versions of the advertisements were also posted on several oncology and/or quality of life list serves. It is projected that the successful applicant will begin the post-doctoral fellowship during the summer of 2005.

#### a. Summary of Activities of Dr. Stephanie Walsh:

Dr. Stephanie Walsh began the post-doctoral fellowship in June of 2003. Her fellowship will end in June of 2005. During the past year, she has completed the following activities:

#### Published Journal Articles:

Matheson, J., Benson, K., Walsh, S.R. (2004). Flattening the hierarchy: The co-creation of an advanced doctoral-level course in feminist-informed family therapy. *Journal of Feminist Family Therapy*, 15(4), 45-74.

Lyness, K., & Walsh, S.R., Sprenkle, D.H. (In Press). Clinical Trials in Marriage and Family Therapy Research. In D. Sprenkle & F. Piercy (Eds.). *Research Methods in Family Therapy*, second edition. NY: Guilford Press.

Walsh, S.R., Denton, W.H. (In Press). Clinical Issues in Treating Somatoform Disorders for Couple Therapists. *The American Journal of Family Therapy*.



Manuscripts Under Review:

Walsh, S.R., Manuel, J., & Avis, N.E. (Revised and resubmitted). The Impact of Breast Cancer on Younger Women's relationships with their partners and children.

McWey, L.M., & Walsh, S.R. (Revised and resubmitted). The impact of an evidence-based pilot curriculum in a marriage and family therapy doctoral program: An exploratory Study.

Walsh, S.R., Brucker, P.S., & Shields, C.G. Attachment Behaviors and Proximity-Seeking in Cancer Patients and their Partners.

Walsh, S.R., Denton, W.H., & Snively, B.M. Demand-Withdraw Patterns in Somatoform Patients and Their Partners.

Manuscripts in Preparation:

Walsh, S.R., Case, D., & Avis, N.E. Changes in Sexual Functioning Following Diagnosis among Younger Women with Breast Cancer.

Manuel, J., Walsh, S.R., Crawford, S.L., Lawrence, R.H., Avis, N.E. Coping Strategies and QOL among Younger Women with Breast Cancer.

Walsh, S.R., Ip, E., and Naughton, M.J. Predictors of Depression Among Younger Women with Breast Cancer.

Published Scientific Abstracts:

Walsh, S.R., Case, D., & Avis, (2004). Changes in Sexual Functioning Following Diagnosis among Younger Women with Breast Cancer. *Psycho-Oncology*, 13 (1).

Peer-Reviewed Poster Presentations:

Walsh, S.R., & McWey, L.M. Perceptions of Evidence-Based Practice in Marriage and Family Therapy. American Association for Marriage and Family Therapy Annual Conference, Long Beach, CA, 2003.

Walsh, S.R., Case, D., & Avis, N.E. Changes in Sexual Functioning Following Diagnosis among Younger Women with Breast Cancer. American Psychosocial Oncology Society (APOS), Orlando, FL, January, 2004.

Walsh, S.R., Case, D., Avis, N.E. Predictors of Sexual Function among Younger Cancer Survivors. Cancer Survivorship: Pathways to Health after Treatment, Washington DC, June, 2004.

Peer-Reviewed Paper Presentations:

Denton, W.D., Walsh, S.R., & Mendenhall, T.J. Couple Therapy for Depression. American Association for Marriage and Family Therapy Annual Conference. Long Beach, CA, October, 2003.

Walsh, S.R., Brucker, P.S. Open Forum: Post-Doctoral Fellowships. American Association for Marriage and Family Therapy Annual Conference, Atlanta, GA, September, 2004.

Denton, W.H., & Walsh, S.R. Fundamentals of Making DSM-IV Diagnoses. American Association for Marriage and Family Therapy Annual Conference, Atlanta, GA, September, 2004.

Professional Memberships:

August 2003-Present	American Psychosocial Oncology Society
August 2003-Present	Collaborative Family Healthcare Association
October 2003-Present	Psychosocial Oncology Group, WFUHS

National Meetings Attended:

American Association of Marriage and Family Therapists (AAMFT), October 2003.  
American Psychosocial Oncology Society (APOS), January, 2004.  
Cancer Survivorship: Pathways to Health after Treatment, Washington DC, June, 2004.  
American Association of Marriage and Family Therapists (AAMFT), September, 2004.

Grants Pending:

NCI  
Mechanism: R21  
Amount: \$358,750  
Title: Effect of Lung Cancer Diagnosis and Treatment on Couples  
PI: Nancy Stark, PhD  
Effort: Co-Investigator, 25% effort

Lance Armstrong Foundation  
Mechanism:  
Amount: \$165,000  
Title: Effect of Lung Cancer Diagnosis and Treatment on the Couple Relationship  
PI: Nancy Stark, PhD  
Effort: Co-Investigator, 25% effort

NCI

Mechanism: R03

Amount: \$143,500

Title: Cervical Cancer Prevention among Latinas (CAPRELA)

PI: Kristie Long Foley

Effort: Co-Investigator, 5% effort

Master's Courses Audited in the Clinical Epidemiology and Health Services Research Master's Program at Wake Forest University:

Medical Outcomes - Fall, 2003

Applied Linear Models – Spring, 2004

Introduction to Statistical Methods – Fall, 2004

Other Educational Activities:

When a Client has Cancer: A Mind, Body, and Spirit Approach. Presented by the Area Health Education Association (AHEA) at the Wake Forest University School of Medicine, (March, 2004).

Community Service Activities:

Walsh, S.R., & McQuellon, R., The Healing Connection: Strengthening the Relationships of Cancer Patients and their Partners. Presented at Cancer Services, Incorporated, Winston-Salem, NC, April, 2004.

Walsh, S.R. Sexual function among younger women with breast cancer. Presented at Cancer Services, Incorporated, Winston-Salem, NC, May, 2004.

**b. Summary of Activities of Dr. Deborah Farmer:**

Dr. Deborah Farmer began the post-doctoral fellowship on September 1, 2003. Her fellowship will end on August 31, 2005. During the past year, she has completed the following activities:

Published Journal Articles: (In the past year)

Mihalko S, Brenes G, Farmer DF, Katula J, Balkrishnan R, Bowen D. Challenges and innovations in enhancing adherence. Controlled Clinical Trials. (In press, 2005).

#### Manuscripts Under Review:

DiBari M, Suggs P, Holmes T, Farmer D, Jackson S. Research partnership with underserved African-American communities to improve the health of older persons. Submitted to Health Reports.

Farmer DF, Bell R, Stark N. Cancer screening and risk factors among Native Americans in eastern North Carolina.

Anderson RT, Weisman CS, Camacho F, Scholle SH, Henderson JT, Farmer DF. Distinguishing satisfaction with on-going health care services from visit-specific ratings in women accessing primary care.

#### Manuscripts In Preparation:

Farmer DF, Ip E, Naughton M. Spirituality and quality of life among young women with breast cancer.

Foley KL, Farmer DF, Smith R, Petronis V, McGraw S, Smith K, Carver C, Avis NE. A qualitative exploration of the cancer experience among long-term survivors: Comparisons by cancer type, gender and age.

Naughton M, Petrek J, Ip E, Case, D, Farmer DF, et al. Quality of life among young women with breast cancer.

#### Grants:

Factors Affecting Breast Cancer Screening Adherence in Older African American Women. Pilot project funded through the PACRE project and the Comprehensive Cancer Center of Wake Forest University. Co-investigator (no salary support) with Dr. Bobbie Reddick of Winston-Salem State University in Winston-Salem, NC. (July 1, 2004 – June 30, 2005).

Cervical Cancer Prevention among Latinas (CAPRELA). An R03 grant submitted to NCI on October 1, 2004. Co-Investigator at 5% effort. Principal Investigator, Dr. Kristie Long Foley, Department of Public Health Sciences, Wake Forest University.

#### Professional Conferences Attended:

International Society for Quality of Life Research in Prague, Czech Republic, November, 2003  
American Psychosocial Oncology Society in Orlando, Florida, January, 2004  
Cancer Survivorship, Pathways to Health After Treatment, Washington, DC, June, 2004

Master's Courses Audited in the Clinical Epidemiology and Health Services Research Master's Program at Wake Forest University:

Introduction to Epidemiology, Fall, 2003  
Advanced Epidemiology and Clinical Trials, Spring, 2004  
Introduction to Statistics, Fall, 2003  
Applied Linear Models, Spring, 2004  
Advanced Statistical Methods, Fall, 2004

Additional Training:

SAS Programming I: Essentials, SAS Institute, Cary, North Carolina, July, 2004  
SAS Programming II: Essentials, SAS Institute, Cary, North Carolina, August, 2004

Professional Memberships:

American Psychosocial Oncology Society (APOS)  
Society for Behavioral Medicine (SBM)

WFU Research Group:

Dr. Farmer is a founder of the Psychosocial Oncology Group (POG), an interest group for post-doctoral fellows and faculty members interested in the psychosocial effects of cancer at the Wake Forest University School of Medicine.

**III. Advisory Board Activities**

No formal advisory board meetings were held during the past grant year. A full advisory board meeting is planned for the spring of 2005 to present center progress to date and develop long-term plans for the breast cancer center of excellence.

**Project 1: Mentrual Cycle Maintenance and Quality of Life After  
Breast Cancer Treatment: A Prospective Study**

## **Abstract**

About 15% of new breast cancer cases occur in women of childbearing age and the majority will be long-term survivors. For those patients who receive adjuvant chemotherapy, almost half will experience amenorrhea, resulting in infertility, menopausal symptoms, and changes in their life quality. The purposes of this study are: 1) to continue to follow prospectively a cohort of 628 young women, ages 18-45, diagnosed with breast cancer, stages 1-3, recruited through a previous award (DAMD17-96-1-6292); and 2) to recruit an additional 200 women from two participating clinical centers (Memorial Sloan-Kettering Cancer Center in New York, and the University of Texas Southwestern in Dallas, Texas). The major objectives of this study are to track the menstrual bleeding patterns of these young women, identify determinants of treatment-related amenorrhea, track subsequent pregnancies and outcomes, examine the women's quality of life longitudinally, and evaluate the patients' disease-free and overall survival. All participants will be followed for a minimum of 2.5 years to a maximum of 8 years. To our knowledge, this is the largest prospective study of young breast cancer patients being conducted in the United States or elsewhere. At 18 months post-diagnosis, 60% of the patients report some menstrual bleeding. Patients also report arm swelling (30%), hot flushes (56%), and vaginal dryness (43%). Patients' life quality is lower during treatment but improves significantly 12-18 months post-diagnosis.

**Subject terms:** breast cancer, quality of life, premature menopause, young women

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## **PART I - INTRODUCTION**

About 15% of new breast cancer cases occur in women of childbearing age and the majority will be long-term survivors. For those patients who receive adjuvant chemotherapy, almost half will experience amenorrhea, resulting in infertility, menopausal symptoms, and changes in their life quality. Very little is known about the incidence, onset, time course, and symptomatology of premature menopause induced by breast cancer therapy, or the impact on the young survivor's quality of life. The purposes of this study are: 1) to continue to follow prospectively a cohort of 628 young women, ages 18-45, diagnosed with breast cancer, stages 1-3, recruited through a previous award (DAMD17-96-1-6292); and 2) to recruit an additional 200 women from two participating clinical centers (Memorial Sloan-Kettering Cancer Center in New York, and the University of Texas Southwestern in Dallas, Texas). The major objectives of this study are to track the menstrual bleeding patterns of these young women, identify determinants of treatment-related amenorrhea, track subsequent pregnancies and outcomes, examine the women's quality of life longitudinally, and evaluate the patients' disease-free and overall survival. All participants will be followed for a minimum of 2.5 years to a maximum of 8 years. To our knowledge, this is the largest prospective study of young breast cancer patients being conducted in the United States or elsewhere.

## **PART II - BODY: STATEMENT OF WORK**

### **Task 1: Continued Follow-up of Study Participants (Months 1-56):**

- a. Clinical Center staff will mail follow-up surveys at 6 month intervals, and menstrual bleeding calendars at 3 month intervals to participants already enrolled in the protocol from the previous DOD award (DAMD17-96-1-6292).**

The coordinating center personnel at Wake Forest University have continued to mail follow-up forms to previously recruited study participants at the prescribed intervals (i.e., bleeding calendars every 3 months; and study questionnaires every 6 months). The total number of participants who were recruited to this study under the previous award is 628 participants. Patients were recruited from the following clinical centers beginning in January of 1998: Memorial Sloan-Cancer Center in New York City (n=450 participants); M.D. Anderson Cancer Center in Houston, Texas (n=92); Wake Forest University (n=49 participants); and Presbyterian Hospital in Dallas, Texas (n=37 participants). Recruitment ended at Wake Forest University, M.D. Anderson Cancer Center, and Presbyterian Hospital in Dallas on December 31, 1999. The current award permits the additional accrual of 200 patients from only two clinical sites: Memorial Sloan-Kettering Cancer Center in New York City, and a new site, the University of Texas-Southwestern Medical Center and its affiliates.

In general, the participants recruited under the former award are well-educated, with 63% having at least a 4 year college degree. Approximately 55% are employed full-time, and 14% are employed part-time, mostly in professional (51%) or managerial positions (17%). Seventy-five percent of the participants are married or are living in a married-like relationship. Roughly

71% of the participants have children. The average age at recruitment to the study was 39 years of age. Approximately 88% of the participants are white (non-Hispanic), 5% are African-American, 4% are Hispanic, and 3% are Asian.

The following table provides information on the current follow-up status of the 628 participants accrued previously:

<u>Participation Status</u>	<u>n</u>	<u>%</u>
Active:	402	64.0%
Completing questionnaires and bleeding calendars	299	74.0%
Completing questionnaires only*	103	25.6%
Dropped/Lost-to-Follow-up:	180	28.7%
Deaths	<u>45</u>	<u>7.2%</u>
	628	100.0%

\* Participants who have had a hysterectomy or who have not had a menstrual period for 2 years post-treatment complete study questionnaires only

Rates of participant dropout have been spread fairly equally across the clinical centers, except for Presbyterian Hospital in Dallas. These patients had to be re-consented in the spring of 2003, and as a result, 9 participants from that site, declined to continue in the study any longer.

	<u>Active</u>	<u>Dropped/Lost to Follow-up</u>	<u>Deaths</u>
Memorial Sloan-Kettering	296 (65.9%)	127 (28.3%)	26 (5.8%)
M.D. Anderson	57 (62.0%)	24 (26.1%)	11 (11.9%)
Wake Forest	31 (63.3%)	15 (30.6%)	3 (6.1%)
Presbyterian Hospital	18 (48.5%)	14 (38.0%)	5 (13.5%)
	402 (64.0%)	180 (28.7%)	45 (7.2%)

Of the 180 persons (28.7%) who have been dropped or lost to follow-up as of November 19, 2004, the following listing provides reasons for study dropouts:

- 75 could not be reached by mail, phone, or personal contacts (i.e., lost to follow-up)
- 69 lost interest in participating in the study any longer
- 7 cited a lack of time
- 5 cancer recurrence or metastatic disease
- 3 illness/treatment side effects/other medical problems
- 4 too overwhelmed to continue participating
- 2 questions too personal/confidentiality issues
- 1 personal/family obligations
- 1 questions were depressing to a participant
- 1 husband asked her to stop participating
- 1 poor English
- 1 upset about her clinical care at her clinical center
- 1 participant began a 2 year sailing trip and asked to be dropped
- 9 patients from Presbyterian Hospital who opted not to be reconsented

In January of 2005, we will begin our 7<sup>th</sup> year of follow-up on our earlier enrolled participants. We have currently retained approximately 64% of our original participants and have lost 7% of our patients to death. Efforts are continuing to try to retain the existing study cohort for another 1.5 years of follow-up. (See Task 6 below.)

**Task 2: Study Set-Up/IRB Approvals (Months 1-12):**

**a. Review procedures already established for study conduct, patient recruitment, and patient follow-up.**

The Manual of Procedures for this study was completed in year 1.

**b. Obtain final IRB site-specific approval for this protocol from the University of Texas Southwestern Medical Center and its affiliates in Dallas, Texas.**

Site-specific IRB approval for the University of Texas Southwestern Medical Center in Dallas, Texas was approved for the Aston Ambulatory Care Center and the Zale Lipshy University Hospital in July of 2001. Approval to accrue patients from the Parkland Health and Hospital System was obtained on September 17, 2001.

**c. Obtain final IRB approval from the DOD for the continued follow-up of previously enrolled participants, as well as for the new recruitment of study participants from Memorial Sloan-Kettering Cancer Center in New York City, and the University of Texas Southwestern Medical Center in Dallas, Texas.**

IRB approval from the DOD was obtained for the continued follow-up of patients originally recruited at Wake Forest University, Memorial Sloan-Kettering Cancer Center, and the M.D. Anderson Cancer Center.

Permission to accrue 200 new patients from the Memorial Sloan-Kettering Cancer Center and the University of Texas-Southwestern Medical Center affiliates was approved in September of 2002.

Approval to re-consent 27 active patients, originally recruited from Presbyterian Hospital in Dallas, to the clinical center at Wake Forest University (Dr. Naughton, Principal Investigator), was obtained in April of 2003. This change was made at the request of Dr. James Strauss (PI) of the Presbyterian Hospital Clinical Center. Participants were sent IRB approved informed re-consent forms and personal health authorization forms. Of these 27 patients, 18 participants agreed to be re-consented, and 9 participants declined to be re-consented for the extended follow-up period. These 9 participants were dropped from our participant tracking system, and no further study materials have been sent to these women.

In August of 2004, Dr. Elizabeth Naftalis, the PI of the University of Texas – Southwestern site left that institution. On September 1, 2004, Dr. Naftalis was replaced as PI by Dr. David Euhus, Associate Professor in the Division of Surgical Oncology at the University of Texas Southwestern.

**Task 3: Patient Recruitment (Months 13-20):**

**a. Identify eligible patients from patient registries at the Memorial Sloan-Kettering Cancer Center and the University of Texas Southwestern Medical Center.**

Staff at the University of Texas-Southwestern Medical Center was trained on September 9, 2002 in procedures of patient identification, patient recruitment, and patient registration by Dr. Michelle Naughton. Staff persons at this site are continually locating eligible patients from patient rosters.

Staff at Memorial Sloan-Kettering in New York continues to identify eligible participants from their hospital billing records and cancer registries. These staff persons worked on the previous award, and thus did not need to undergo additional training.

**b. Begin the recruitment of eligible patients to the protocol. Patients recruited to the protocol from the clinical centers will be registered online using a web-based system developed by the Biostatistic's Core Facility.**

As of November 10, 2004, an addition 171 patients have been recruited to the study. Study coordinators at Memorial Sloan-Kettering have recruited 155 participants. The University of Texas-Southwestern Medical Center has recruited 16 patients. These patients have been registered on-line, using the new registration system developed by the Biostatistic's Core. Thus we have achieved 85.5% (171/200) of our recruitment goal. An additional 29 participants will

be recruited to this protocol. Recruitment to this protocol was delayed during the first 2 years of the funding period, pending DOD IRB approval of the protocol. Thus, recruitment will be completed during the next 12 months of the funding period.

**c. Clinical Center staff will mail baseline, eligibility, and screening forms to the Coordinating Center at Wake Forest University.**

Study coordinators at Memorial Sloan-Kettering and UT-Southwestern have mailed the baseline, eligibility, and screening forms to the project managers at the coordinating center at Wake Forest University. Copies of these forms also remain in the patients' files at Sloan-Kettering and UT Southwestern, along with the original copy of the signed informed consent forms. Wake Forest University does not keep copies of the patients' consent forms.

**Task 4: New Patient Follow-up (Months 13-56):**

**a. Coordinating Center will mail out bleeding calendars every 3 months, and follow-up questionnaires every 6 months to the newly enrolled participants.**

The recruited patients have been entered into the study tracking system, and receive bleeding calendars and questionnaires from staff at the coordinating center at the above specified intervals.

Seven of the 171 participants or 4.1% have dropped since enrollment. The reasons for participant dropout are as follows:

- 2 – no longer interested
- 2 - cannot be reached
- 1 - overwhelmed
- 1 - too much paperwork
- 1 - death

**b. Clinical Center staff will complete the Chart Review Form at 12 months post-recruitment on the newly enrolled patients.**

All new participants recruited to the study have Chart Review Forms completed at 12 months post-recruitment. Staff at the participating clinical centers are notified as to when chart review forms are due. Completed forms are mailed to the Project Manager at Wake Forest University for data entry.

**Task 5: Data Cleaning and Management (Months 1-57):**

**a. Biostatistic's Core will perform all data-related tasks, including devising the patient registration, data entry and data management systems. SAS data sets will be developed for interim and final analyses of study data.**

The Biostatistic's Core Facility has completed the following tasks for this protocol in the past year:

- 1) continued to develop a data entry system for both the new and the old study data.
- 2) provided a series of error reports to assist in data cleaning and maintaining data quality.
- 3) prepared interim analyses of study data.
- 4) maintained SAS data sets of collected study data.
- 5) completed data analyses of participant menstrual bleeding, arm and hand swelling, quality of life, and sexual satisfaction and arousal.

Further details about the activities of the Biostatistic's Core can be found in the annual report document from the core facility.

**b. Data cleaning will be performed by the Project Manager's in conjunction with the Biostatistic's Core programmers.**

Data cleaning continues on a regular basis in conjunction with the study programmers. Project managers review all baseline and follow-up study forms as they are received from the clinical centers and the study participants, respectively, in order to check for errors or missing data. Participants are contacted if questions about the study forms arise.

**Task 6: Adherence and Retention (Months 1-56):**

**a. Receipt of participants' bleeding calendars and forms will be tracked by staff at the Coordinating Center.**

All enrolled patients are entered into our study tracking system, which cues our study staff when follow-up forms and bleeding calendars are to be mailed to participants. Patient forms are mailed approximately 3 weeks prior to their target completion date in order to allow time for participants to receive the forms in the mail and complete them in their homes. Participants who have not returned their study forms within 14 days of their target completion date, are sent a reminder post-card regarding the study forms. If the forms have still not been received within 22 days of their target completion date, these participants are called by our Assistant Project Manager to inquire regarding the status of the forms. The Assistant Project Manager works with individual participants who are having difficulty completing study forms, for whatever reason, to try to make the completion of the study requirements as easy as possible.

Patient compliance among the active participants in completing study questionnaires and monthly bleeding calendars is approximately 80%- 85%.

Study project managers also check all follow-up questionnaires completed by participants to check whether scores on the Beck Depression Inventory are within normal ranges. During the past 12 months, 11 patients achieved Beck Depression scores above the cutoff score of 15

points. The PIs of the participants' respective institutions were contacted, and the participants were referred to health professionals and/or support groups, if they were not already seeking assistance in controlling depressive symptoms. No adverse outcomes have occurred with any of these 11 patients.

**b. Incentives for maintaining high levels of patient participation in follow-up activities will continue to be devised.**

Retention of study participants is paramount in the current protocol. All participants will be followed for a minimum of 3.5 years to a maximum of 8.5 years. Participants receive no monetary compensation for their participation, but donate their time in completing the study requirements. In addition, the study participants are located in 20+ states in the United States, and two other countries, with no face-to-face contact with study coordinators after their initial study recruitment. Thus, there is no means to reinforce, in-person, the importance of study participation outside of mailed contacts with study staff.

Current Retention Activities Used:

Study Newsletters – are printed and mailed to all study participants on a regular basis. These letters provide updates on study participation, new information regarding issues related to breast cancer, and a “Participant Corner” in which individual participants have volunteered to share their cancer experiences with the other participants. Recently, information has been provided regarding the study results to participants who are 3 years or more beyond their date of recruitment. (See Appendix A.)

Tokens of Appreciation – all participants receive tokens of appreciation 1-2 times per year. In the past, these gifts have included: pens, refrigerator magnets, memo pads, pamphlet on lymphedema issues, and a book on breast cancer treatment co-authored by our Co-Principal Investigator, Dr. Jeanne Petrek. This fall, participants will receive a copy of: *You Are Not Alone: A guide and Resource Directory for Young Women with Breast Cancer*, compiled by the Young Survival Coalition of the American Cancer Society.

Birthday Cards – all participants are sent cards on their birthdays each year.

Special Event Cards - participants are sent cards to celebrate special events in their lives, that they share with us, including weddings, births, receiving a promotion, etc. Similarly, sympathy cards are sent to participants who have experienced a loss, and to the spouses/partners/relative of a study participant who has died.

Quarterly Drawings for Gift Certificates - Quarterly drawings of gift certificates were initiated approximately 3 years ago, to provide an additional “boost” to study participation. Study drawings are conducted using the following procedure:

All participants receive some type of mailing (i.e., bleeding diaries or bleeding diaries plus a study questionnaire) from the study coordinating center each quarter. Participants are

informed that by returning their diaries and/or questionnaires by the due date listed on the label attached to their forms, that they will be automatically included in a quarterly drawing for gift certificates. Once the participants' packets are mailed back to the coordinating center, the extra ID labels attached to their study forms are cut off by Ms. Carol Corum, the study Project Manager, and are stored in large envelopes designated for the participants' initial recruitment site (i.e., Memorial Sloan-Kettering; Wake Forest; Presbyterian Hospital; M.D. Anderson Cancer Center). At the end of each quarter, seven winners are selected in the following proportions to match the number of participants at each clinical center: 4 winners from Memorial Sloan-Kettering, 1 from Wake Forest, 1 from the patients originally registered through Presbyterian Hospital in Dallas, and 1 from M.D. Anderson Cancer Center. No participants are allowed to receive a prize more than once, and if a repeat winner is drawn, another label is drawn from that site.

After a winner has been drawn, Ms. Corum calls the participants to inform them that they have won the quarterly drawing and to see if they would like to accept a gift certificate. (Only 3 women have declined a gift certificate since the initiation of this incentive.) Participants may choose a gift certificate from: Home Depot, Lowe's Home Improvement, Walmart, or a Long-distance calling card. Because our participant population is geographically diverse, we have chosen large retail chains, so that most participants have 2 or more of these stores in their area from which to choose.

In the past year, 28 women have received \$50 gift certificates from one of these retail stores.

To date, the participant drawings have gone smoothly, and we have received no complaints from any participants regarding the conduct of these drawings. We are continuing to seek out new ways to provide incentives to the participants in this study, but the drawings have motivated many participants to return their study forms in a timely manner. We believe that the incentives will continue to be more important as new recruitment of participants will be occurring over the next 12 months, as well as the continued follow-up of study participants, some of whom have already been enrolled in the protocol for almost 7 years.



- c. A study newsletter will continue to be written and sent to all patients at least twice a year.**

Study newsletters were sent to all participants in December of 2003 and May of 2004. At each of these time points, one newsletter, which contained some preliminary results of the study data, was provided to participants who were 3 or more years beyond study recruitment. A different newsletter, which contained no major study results, was provided to participants who have been recruited less than 3 years. Study results were provided through 36 months post-recruitment only to those who had completed the 36 month follow-up form in order to avoid "coloring" the responses of participants who had not yet reached that assessment point. The rationale for including some information about study results is that the newsletters provide another means of giving feedback and information to the participants for their lengthy participation in the trial. (See Appendix A.)

A study newsletter is being developed currently for distribution in December of 2004.

- c. Birthday cards will be mailed to all participants.**

Birthday cards were mailed to all active study participants on their birthdays during this past year.

- d. Holiday cards will be mailed to participants every December.**

A holiday greeting was included in the December, 2003 newsletter. (See Appendix A.)

A Valentine's Day mailing was also completed in February of 2004. (See Appendix B.)

**Task 7: Data Analyses/Manuscript Preparation/ Presentations (Months 6-57):**

- a. Abstracts, manuscripts and posters will be prepared from interim data (i.e., data sets comprised of participants 1, 2, 3, and 4 years post-recruitment).**

Abstracts and poster presentations completed during this past grant year:

None.

Data Analyses:

Data analyses has been a major activity of the grant since the spring of 2004. Several manuscripts have been developed on the following topics: menstrual bleeding from diagnosis through up to 5 years of patient follow-up; participant health-related quality of life from diagnosis through 3 years post-diagnosis; patterns in arm and hand swelling from baseline through 3 years of follow-up; and sexual satisfaction and arousal at 1 year post-surgery. (See Appendix C for summaries of these results.)

**b. Annual reports will be written to the DOD.**

The annual report to the DOD reviewing the activities of their protocol over the past year was prepared in November, 2004.

**Task 8: Final Analyses and Report Writing, (Months 54-57):**

**a. Final analyses of data assessing primary study endpoints will be performed, and manuscripts will be written and submitted for publication in peer-reviewed journals.**

Task not applicable at this time.

**PART III - KEY RESEARCH ACCOMPLISHMENTS**

- 771 women have been recruited to this protocol since 1998, (171 have been recruited under the new award. Retention of the entire study cohort is approximately 64% after up to 82 months of study follow-up. Retention of the newly recruited participants is 95.9% (164/171 participants).
- Risk factors for breast cancer among these women: 17% of the participants had a mother or a sister with a prior diagnosis of breast cancer; 39% of the participants had their pregnancy at age 30 or above; and 35% were regular smokers at the time of diagnosis (average number of years smoking = 9.7; range 3-15 years).
- Type of surgery: 51% had a lumpectomy; 49% had a mastectomy
- Type of cancer treatment: chemotherapy and radiation 62%; chemotherapy alone 25%; radiation only 8%; no active treatment begun at diagnosis; hormonal treatment following active treatment: 57%.
- Menstrual bleeding patterns: Approximately 43% of patients were having some menstrual bleeding at approximately 1 year following the end of treatment. Bleeding was highest for those patients who received no chemotherapy, and those who were younger (< 35 years of age) at the time of diagnosis.
- With respect to chemotherapy regimen, menstrual bleeding was highest for those receiving adriamycin and cyclophosphamide (AC), and lowest for those receiving adriamycin, cyclophosphamide and docetaxel (ACR) or cyclophosphamide, methotrexate, and 5-fluorouracil (CMF).
- Menopausal symptoms: At 18-24 months post-diagnosis, approximately half of the participants are reporting some menopausal symptoms. For example, 56% of the

patients report hot flushes, 46% report night sweats, 43% report vaginal dryness, 68% report restless sleep, and 63% report mood changes. Reporting of vasomotor symptoms has been increasing during the follow-up period as the participants age and menstrual cycles decrease.

- Pregnancy outcomes: Patients have reported 69 pregnancies during the follow-up period resulting in 44 live births (including 2 sets of twins).
- Health-related quality of life: Overall, patients' health-related quality of life has been improving as time from diagnosis and treatment increases. Predictors of better quality of life at 1 year post diagnosis are: Caucasian ethnicity, having greater satisfaction with physical appearance, having greater social support, and time since diagnosis. At 2 and 3 years post diagnosis, however, educational level, chemotherapy and moderate exercise also become significant predictors of overall quality of life. Participants who are more highly educated and engage in moderate weekly exercise report better quality of life. Receiving a form of chemotherapy, however, is found to be a negative predictor of quality of life at 2 and 3 years post-diagnosis.
- Sexual Functioning: Approximately 82.7% of participants report being sexually active at approximately 1 year post-surgery for their breast cancer. Participants who were not sexually active tended to be married or partnered, to have a smaller tumor size at diagnosis, and to report higher quality of life and social support, and fewer depressive symptoms than those who were sexually inactive.
- Higher sexual arousal at 1 year post-breast cancer surgery was found to be significantly related to having menstrual bleeding, a higher body mass index (BMI), better sleep quality, greater satisfaction with one's physical appearance, and not avoiding physical affection.
- Higher sexual satisfaction at 1 year post-breast cancer surgery was found to be significantly related to having menstrual bleeding, reporting fewer depressive symptoms, greater satisfaction with one's physical appearance, and not avoiding physical affection.

#### **PART IV - REPORTABLE OUTCOMES**

##### 1) Abstracts and poster presentations completed during this past grant year:

None

##### 2) Published Journal Articles:

None.

## **PART V - CONCLUSIONS**

Further data analyses are planned during 2004-2005 to examine changes in patients' health status, bleeding patterns, menopausal status, pregnancies, and health-related quality of life post-treatment. Sample sizes are now sufficient at 3 years post-diagnosis to enable us to begin publishing findings from this research study in scientific journals.

The results of this research will enable us to answer critical questions regarding the risks (or non-risks) of childbearing after breast cancer, will assist in predicting which women may be more likely to lose their menstrual cycles following breast cancer treatment, and will provide much needed, longitudinal data on the quality of life of young cancer patients following treatment from breast cancer. Few studies have examined the impact of breast cancer diagnosis and treatment on young women long-term. Younger women are at a different life stage than patients in their 60's and 70's, and face different kinds of challenges than older women. Issues such as caring for children in the home, balancing work and family roles, and changes in physical health as a result of cancer or its treatment, (e.g., lymphedema or premature menopause), are concerns of importance to young survivors. The development of interventions to assist women in maintaining optimal quality of life following treatment is critical.

## **PART VI - REFERENCES**

N/A

**Project 2: Investigating Mechanisms to Explain Age Associated  
Differences in Quality of Life Among Breast Cancer Patients**

## **Abstract**

The primary purpose of this study is to examine mechanisms that may explain age differences in the health-related quality of life of women who have been diagnosed with a first-time breast cancer. The study will examine psychosocial factors such as social support, coping strategies, resiliency, and the impact of cancer on life responsibilities as explanations of age-associated factors affecting HRQL. This project is an observational, longitudinal study of women aged 18 and over who are newly diagnosed with breast cancer. In order to examine both the short- and longer-term impact of breast cancer on HRQL, the study will survey women post diagnosis and follow them at 3, 6, 12, and 18 months. A secondary purpose of the proposed study is to have this large cohort of breast cancer patients serve as a comparison group for the other studies in the Behavioral Center of Excellence. Patients for the proposed study will be recruited from two clinical centers: Memorial Sloan-Kettering Cancer Center (MSK) and University of Texas - Southwestern University (UT-SW).

**Subject terms:** breast cancer, quality of life, aging

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## **PART I - INTRODUCTION**

The primary purpose of this research is to examine mechanisms that may explain age differences in the health-related quality of life of women who have been diagnosed with a first-time breast cancer. The study examines psychosocial factors such as social support, coping strategies, resiliency, and the impact of cancer on life responsibilities as explanations of age-associated factors affecting HRQL. This project is an observational, longitudinal study of women aged 18 and over who are newly diagnosed with breast cancer. In order to examine both the short- and longer-term impact of breast cancer on HRQL, the study surveys women post diagnosis and follow them at 3, 6, 12, and 18 months. A secondary purpose of the study is to have this large cohort of breast cancer patients serve as a comparison group for the other studies in the Behavioral Center of Excellence. Patients for the study are being recruited from two clinical centers: Memorial Sloan-Kettering Cancer Center (MSK) and University of Texas - Southwestern University (UT-SW).

## **PART II – BODY: STATEMENT OF WORK**

The primary activities during this third year of the study have been to continue study recruitment and follow-up at Memorial Sloan Kettering Cancer Center and to begin recruitment and follow-up at University of Texas- Southwestern. The tasks described in the original statement of work have not changed. However, time involved in obtaining Human Subjects approval from the Department of Defense was not included as part of the original timeline. This approval has taken an enormous amount of time and has essentially moved the timeline back over a year. Because of these delays, last year we received additional funding for a 5<sup>th</sup> project year. It is important to note that we did not receive Human Subjects approval from the Department of Defense to recruit at University of Texas- Southwestern (UT-SW) until February 2004. Thus, we have only been recruiting at UT-Southwestern for 8 months. We did not receive approval to recruit from Memorial Sloan Kettering until April 2003 and have thus been recruiting from this site for 18 months. These delays have had a significant impact on our ability to reach our targeted recruitment.

### **Task 1: Develop research protocol (months 1-15)**

#### **a. Finalize research questionnaires**

The questionnaires were finalized and submitted with the 2002 report.

#### **b. Review protocol with sites**

As stated above, the protocol has been reviewed and approved by the IRBs at all sites. The DOD Office of Human Subjects Protection approved the protocol for Memorial Sloan Kettering Cancer Center in April 2003 and they approved the protocol for the University of Texas – Southwestern in February 2004.

### **Task 2: Develop data management system (months 3-12)**

#### **a. Develop data management requirements**



- b. Develop reporting requirements
- c. Develop contact record
- d. Train data manager

These tasks have all been completed. Please see the Biostatistics Core Report for a review of these ongoing activities.

**Task 3: Identify, recruit, and conduct baseline interviews of eligible patients (months 16-33)**

- a. Study sites identify and recruit eligible patients
- b. Patients recruited and interviewed

Recruitment has begun at both sites. As of October 31, 2004, 408 women have been recruited into the study. Because of the delays in obtaining Human Subjects Approval from DOD we are extending recruitment into 2005. Please see the below table for a distribution by age of study participants.

**Table of Study Recruitment by Age Category as of October 31, 2004**

Ages 18-45 (No menstrual bleeding)	Ages 18-45* (Menstrual Bleeding)	Ages 46 – 54 years	Ages 55 – 64 years	Ages 65+ Years	Total
1 .2%	107 26.4%	116 28.1%	102 25.1%	82 20.2%	408 100%

\* Participants in the age 18-45 (menstrual bleeding) category are shared with Project 1: Menstrual Cycle Maintenance and Quality of Life Following Breast Cancer Treatment.

- c. Quality control (ongoing)

Quality control is an ongoing activity. See the Biostatistics Core Report for a review of these ongoing activities.

- d. Medical record review

Medical record review is being conducted at both sites 12 months from the date of the participants' recruitment. This is ongoing.

- e. Data entry system developed

This task has been completed for both sites.

- f. Data entry of questionnaires (ongoing)

This task is being completed for the recruited participants.

#### Task 4: Ongoing follow-up of patients (months 19-52)

- a. Tracking of women in study
- b. Mailing of follow-up questionnaires

All women who have been recruited have been entered into a tracking data base. Follow-up forms are mailed at 2 ½, 5 ½, 11, and 17 months following baseline – for the 3- and 6-, 12 and 18- month follow-ups. To date, only 7 women (1.7%) have dropped out of the study; none of these were in the 18-45 age range and 7 participants were over age 45. Reasons for study drop-out were:

Not interested (3)  
Illness/treatment side effects (1)  
Could not be reached (1)  
Death (1)  
With Hospice (1)

The following table shows the number of follow-up interviews completed to date:

	3 mo. FU		6 mo. FU		12 mo. FU		18 mo. FU	
	N	%	N	%	N	%	N	%
Due	4	1.0%	3	0.7%	2	0.5%	7	1.7%
Due and out of window	21	5.1%	20	4.9%	14	3.4%	3	0.7%
Due and booklet returned	339	83.1%	246	60.3%	174	42.6%	39	9.6%
Not due	42	10.3%	137	33.6%	217	53.2%	354	86.8%
Not due-booklet returned	2	0.5%	2	0.5%	1	0.2%	5	1.7%
Total	408		408		408		408	

- c. Contacting non-responders

Women who do not return their survey by the due date are sent a postcard reminder. Follow-up phone calls are made if forms are not received one week after the due date.

- d. Mailing of incentives

To date, we have mailed out 13 gift certificate incentives. No one has refused a gift certificate.

- e. Follow-up medical record reviews

This has not been completed as the study forms are not yet due.

**Task 5: Data Analysis and Report Writing (months 33-60)**

- a. Merging of data management, questionnaire, and medical record files
- b. Data cleaning
- c. Data analysis
- d. Presentation of results at professional meetings
- e. Initial manuscripts prepared

None of these tasks have begun as they are not yet due.

**Part III - KEY RESEARCH ACCOMPLISHMENTS**

- Finalization of study forms
- Obtaining human subjects protection approval for study initiation at Memorial Sloan-Kettering and University of Texas - Southwestern University
- Beginning study recruitment and follow-up at Memorial Sloan-Kettering and University of Texas - Southwestern University.

**PART IV - REPORTABLE OUTCOMES**

none

**Part V - CONCLUSIONS**

This section is not applicable at this point.

**PART VI - REFERENCES**

Not applicable

**Project 3: Research on Optimal Recovery Practices in Breast Cancer  
(RESTORE)**

## **Abstract**

Breast cancer is one of the most prevalent diseases among women, and one of the most feared. Although society has benefited from advances in medical and surgical treatments leading to increased survivorship, there has been a general lag in the development of post treatment health care programs to improve the quality of life for women following breast cancer. RESTORE focuses on two issues post-surgery that affect the lives of women with breast cancer: quality of life and lymphedema. There is now ample data in the literature on fatigue, emotional distress, and the recovery phase from the diagnosis of cancer and its treatment to conclude that for at least some women psychosocial issues may be significant and lasting posing additional barriers to recovery from cancer. Further, as the majority of women now receive axillary node dissection, risk for lymphedema (swelling of the arm), leading to pain, psychological distress, and impairment of physical, vocational, social and sexual functioning is increasingly important. The goal of this project is to test whether a combined intervention program can improve health-related quality of life and physical functioning for women newly diagnosed with breast cancer. This program is a tailored exercise program, which includes a lymphedema prevention program, and patient education. Results from this study will be used to recommend post-operative cancer care strategies to enhance well-being and quality-of-life for women.

**Subject terms:** breast cancer, quality of life, lymphedema prevention, exercise

**Project 3**  
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## **Part I – INTRODUCTION**

[Original Abstract] Breast cancer is one of the most prevalent diseases among women. Although advances in medical and surgical treatments have led to increased survivorship, there has been a general lag in the development of post-operative health care programs. This research project tests an intervention (with a control group) designed to enhance the health and well-being of adult women of all ages recently treated for breast cancer in the Piedmont Triad region of North Carolina. We will randomize 200 women with stages I to III breast cancer 100 to each of the following: (1) usual care consisting of patient education, and 2) a comprehensive program of tailored exercise. Identification of eligible women will occur through medical and surgical oncologists' offices and through the WFU Comprehensive Cancer Center. Age and stage eligible women will be enrolled 2 to 12 weeks post surgery and followed for 18 months. The exercise programs are center-based and tapered to home sessions to promote high adherence levels by integration into daily life. The Comprehensive Tailored Exercise Program focuses on improving muscle strength and flexibility, and the swelling prevention program focuses specifically on arm exercises, massage techniques, and wearing of an elastic sleeve. Outcomes include change from baseline in the 6-minute walk test, the FACT-B (Functional Assessment of Cancer Therapy – Breast) health-related quality of life scale, and swelling during the 18-month period following randomization.

## **Part II – Body: ORIGINAL STATEMENT OF WORK**

### **Task 1. Identify, contact, and recruit 200 eligible women.**

- a. Recruit and consent eligible patients into the study (a 28-month period inclusive of months 09-36).

Status: Recruitment began on October 28, 2002 and has been underway approximately 24 months. Initially, we experienced lower yields than what was forecasted. We have made modifications to our protocol which involved dropping the lymphedema outcome and thus, widening the window and criteria for recruitment.

As of October 30, 2004, we have randomized 77 women into RESTORE, and have 7 scheduled for randomization in November. In addition, 11 women have dropped out of the study, 10 due to time constraints and 1 participant for a lack of interest. We have modified our protocol twice to improve recruitment yields. First, we extended eligibility to women with sentinel node procedures and, therefore, no longer restrict eligibility to patients having undergone axillary node dissection. The latter modification was necessary to reflect trends in surgical management of breast cancer which have moved away from routine full axillary node dissection. In years prior to RESTORE, we estimated from clinical data that as many as 80% of women with invasive stage breast cancer would undergo full axillary node dissection. More recently, we have observed a much lower rate of axillary node dissection (< than 30%). We have also recently modified our protocol to offer a combined baseline 1 and 2 visit. This combination will allow us to continue to recruit otherwise eligible women who were unable to attend the first baseline visit within the time-window. The combination of baseline visits 1 and 2 will not affect the timing of the baseline 2 visit, and thus will not affect data analysis

and interpretation. We have extended recruitment to satellite clinics of the participating institutions, and currently plan to add recruitment at High Point Regional Medical Center, which is an approximately 20 minute drive from Winston-Salem. The latter new site, if added, would require IRB approval. We have added a pre-signed doctor's letter to eligible patients following breast cancer surgery, which is mailed to the patient upon ascertainment of eligibility status. Finally, we have added a \$10 finder's fee for clinic office staff who recruit participants to RESTORE. The fee is consistent with the stipend received by office staff from other studies.

Our current recruitment yields are now approximating 4 per month, which we believe is likely to be near the prevailing maximum rate given our population base. We anticipate that the number recruited over the remaining months will be sufficient to address our primary aims of investigating fitness and quality of life effects of the intervention relative to controls, for which we need approximately 100 participants. A protocol amendment to remove lymphedema as an outcome and reduce the sample size for RESTORE accordingly to N=100 subjects was approved by WFUSM Institutional Review Board, and by the project office (DoD) in March and April of 2004. The revision was formally enacted by approval by the RESTORE DSMB in May 2004. RESTORE will retain the ability to statistically determine if the exercise intervention is associated with changes in arm swelling. All future progress reports and documentation will now reflect the revised sample size and study objectives; no other changes were made to the Statement of Work.

We have developed a RESTORE newsletter and a quarterly speaker series providing information on cancer topics for the purpose of keeping contact with those randomized to the control group.

To secure optimal retention in both control and intervention arms of RESTORE we have recently implemented an incentive program, as described in Appendix D.

#### **Task 2. Conduct Baseline 1 visit.**

- a. Schedule participant visits to Reynolda Campus for baseline visit 1 to assess fitness and Health-Related Quality of Life (HRQL).

Status: Study investigators and staff continue to schedule and hold Baseline 1 visits as directed by the protocol. We have not encountered any problems in this regard.

#### **Task 3. Conduct 3-month visit: Baseline 2.**

- a. Assess QOL, fitness, swelling, anthropometrics and health status.

Status: Study investigators and staff continue to schedule and hold Baseline 2 visits as directed by the protocol. We have not encountered any problems in this regard.

- b. Assess resting metabolism and diet at GCRC.

Status: RESTORE time slots for testing at the GCRC are ongoing.



- c. Conduct baseline DEXA scan (months 5-30).

Status: RESTORE time slots for testing at the GCRC are assigned as needed.

**Task 4. Conduct Tailored Exercise Program (CTEP) to CTEP group.**

- a. Develop and begin tailored physical activity.

Status: Study interventionists and staff are continuing to administer the planned comprehensive behavioral intervention designed to encourage self-monitoring of exercise and nutritional habits in order to increase desired nutritional and exercise behaviors. The behavioral intervention was piloted in conjunction with a pilot exercise intervention. Information gained during the pilot intervention was used to modify the current intervention. Intervention staff has researched current practices in group interaction, motivational interviewing, and goal setting in order to provide more effective group leadership and motivation.

**Task 5. Conduct 6-month follow-up visit.**

- a. Assess QOL, fitness, swelling, anthropometrics and health status.

Status: The 6-month follow-up visit is similar in scope to the Baseline 2 visit. These visits are being scheduled and held as planned.

**Task 6. Conduct 9-month follow-up visit. End center-based exercise phase.**

- a. Assess QOL, fitness, swelling, anthropometrics and health status.

Status: The 9-month follow-up visit is similar in scope to the Baseline 2 visit. These visits are being scheduled and held as planned.

- b. Begin home-based exercise phase.

Status: Interventionists have developed information to distribute to participants prior to beginning the home-based phase of the exercise program. Methods of monitoring activity level have been established and are utilized when participants reach this phase of the intervention.

**Task 7. Conduct 12-month Telephone Call.**

- a. Assess Fatigue and HRQL.

Status: Calls are ongoing as planned.

**Task 8. Conduct 15-month follow-up visit. (months 18-44).**

- a. Assess QOL, fitness, swelling, and health status.

Status: The 15-month follow-up visit is similar in scope to the Baseline 2 visit. Staff has been trained to perform both physical and psychosocial assessments for this visit.

- b. Assess diet assessment and DEXA components.

Status: These measures are ongoing as scheduled.

**Task 9. Conduct final visit. (Months 21-47).**

- a. Assess QOL, fitness, swelling, and health status.

Status: The final testing visit is similar in scope to the Baseline 2 visit. Staff has been trained to perform both physical and psychosocial assessments for this visit.

- b. Assess resting metabolism and diet at GCRC.

Status: Assessments of follow-up measures are ongoing as planned.

- c. Conduct DEXA scan.

Status: Assessments are ongoing as planned.

**Task 10. Create analytic database.**

- a. Develop study forms for web-based data entry.

Status: Data collection forms have been designed in a manner that allows for web-based data entry. Computer programmers have worked closely with investigators and study staff to insure that the web-based data-entry site is user-friendly and is currently being used for data-entry without any problems.

Study investigators have assisted with the development of web-based calendar and scheduling systems that integrate all of the RESTORE activities. This system issues reminders, flags, and alerts based upon the timeliness of the completion of key study visit activities.

### **Part III. KEY RESEARCH ACCOMPLISHMENTS**

- Refined recruitment methods to include pre-signed letter from oncologist; added satellite clinics; implemented corridor/waiting room posters describing RESTORE; increased placement of brochures; and held monthly visits with physician groups to ensure full cooperation in accessing patients.
- Obtained all IRB and DOD human subjects protocol modification approvals.
- Staffed public awareness booths for RESTORE at local public breast cancer awareness activities.
- Implemented incentives for participants.
- Convened a DSMB meeting in May 2004. No safety concerns were noted. Our next DSMB meeting is scheduled for December 3, 2004.
- To date, 12 participants have completed the study. 55 participants have completed the 6 month visit.

### **Part IV. REPORTABLE OUTCOMES**

#### Adverse Events

We have reported 39 adverse events, of which 4 were SAEs. None of these events were determined to be likely related to RESTORE. IRB filings have been made for each case.

#### Abstracts, Posters, Manuscripts

None

**Part V. CONCLUSIONS**

N/A

**Part VI. REFERENCES**

N/A

## **Biostatistics Core Facility**

## **Abstract**

The overall objective of the Biostatistic's Core Facility for this Behavioral Center of Excellence is to collaborate with investigators in each project throughout all phases of the research. Major responsibilities are assumed for statistical, methodological, logistical, and computer related issues including study design, data collection, quality control, database development and management, data analysis, and manuscript preparation, each of which is vitally important to the success of the BCE. The Core Facility has been and will continue to be involved in all phases of these projects. Staff members have collaborated with individual investigators in defining objectives for each research project, defining end points to quantify treatment effect, selecting appropriate information for data collection, determining sample sizes that ensure adequate power, and developing randomization schemes that ensure valid treatment comparisons. The Core Facility will continue to be involved in these studies during their execution and analysis.

**Subject terms:** breast cancer, quality of life, data management, data analyses

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## **PART I - INTRODUCTION**

The overall objective of the Biostatistics Core Facility for this Behavioral Center of Excellence is to collaborate with investigators in each project throughout all phases of the research. Major responsibilities are assumed for statistical, methodological, logistical, and computer related issues including study design, data collection, quality control, database development and management, data analysis, and manuscript preparation, each of which is vitally important to the success of the BCE. The Core Facility has been and will continue to be involved in all phases of these projects. Staff members initially collaborated with individual investigators in defining objectives for each research project, defining end points to quantify treatment effect, selecting appropriate information for data collection, refining data collection forms, determining sample sizes that ensure adequate power, and developing randomization schemes that ensure valid treatment comparisons. Subsequently, staff members have collaborated with the investigators in designing and programming a web-based data entry and tracking system, implementing quality control features, and performing preliminary analyses. The Core Facility will continue to be involved in these studies during their execution and continuing analysis.

## **PART II – BODY: STATEMENT OF WORK**

### **Task 1: Study Design (Month 1)**

- a. Help formulate primary and secondary study hypotheses and define important outcome variables;**
- b. Determine sample sizes that ensure adequate power;**
- c. Develop randomization schemes that ensure valid treatment comparisons.**

Completed in Year 1

### **Task 2: Protocol and Form Development (Months 2 – 3)**

- a. Assist with the development of Manual of Operations. Manuals of Procedure will be developed which will clearly define all procedures and contingency plans. All procedures will be tested before accrual of any patients.**
- b. Help develop concise, easily understood data collection forms. Assess their inter- and intra-tester reliability.**

Completed in Year 1



### **Task 3: Database Setup (Months 4 - 10)**

- a. Design and implement a computer database management system. A computer database will be established that allows web-based data entry.**
  - b. Design and implement quality control procedures for data checking, storing and updating data while maintaining security and confidentiality.**
- Completed the design of the web-based database during year 1. During the last year, this database was maintained and enhanced with additional functionalities.
  - The study management/tracking systems for the Menstrual Cycle Maintenance (Project 1) study, the Age Differences (Project 2) study, and the RESTORE study (Project 3) were completed in Year 2. During the last year, these systems were maintained and enhanced with additional functionalities based on end-user feedback using ColdFusion and Microsoft SQL Server relational database management software.
  - For the Menstrual Cycle Maintenance (Project 1) and Age Differences (Project 2) studies, web-based data entry facilities were completed for the baseline visit booklet and the 6, 12, 60 and 72 month follow-up surveys (surveys for 36 and 48 month follow up were completed last year); quality control features were built into the screens (e.g., range checks, field checks, skip patterns, etc.); validation error reports were implemented, displaying outstanding errors for all forms, by Participant ID. Work continues on data entry facilities for the chart review form and the 18 and 24 month follow-up form booklets. For Project 3, web-based data entry facilities were completed for 31 forms for the Baseline, 3, 6, 12, 15, and 18 month follow-up visits; quality control features are currently being built into the screens (e.g., range checks, field checks, skip patterns, etc.) and validation error reports are nearing implementation. Also, batch processing of errors will be implemented to check for errors in all the data that has been entered to date, prior to real-time error checking implementation. In addition, maintenance and enhancements to the participant visit scheduling and mailing tracking systems for Project 3 continue based on end-user requirements. End of study mailings, participant fitness feedback reports, recruitment reports, and a dropped participants report were implemented.
  - Maintained security measures on data collected in all three projects. All data entered into the web site is saved onto a secure database server located in the Department of Public Health Sciences. The server is located behind the Wake Forest University Health Sciences' firewall and the data is backed up to tape nightly. These tapes are stored onsite in a fireproof cabinet for 2 weeks, after which they are moved offsite. Offsite, the tapes are stored in a lock box, in a vault, maintained by WFUSM Information Services. The web site utilizes Secure Socket Layer Encryption software to encrypt data moving to and from each user's PC. Website security authorization will be enhanced to comply with HIPAA regulations in the next 3 months, requiring greater password strength and periodic password change to ensure restricted access the web site and study data. Access to each area of the web site is determined by access privileges based on role and is stored in a SQL Server database.

**Task 4: Data Management (Months 11 – 40)**

- a. Perform interim analyses and provide feedback to the investigators regarding patient accrual and quality control.**
- b. Tabulate and summarize measures of protocol adherence and numbers of dropouts for coded treatment group assignment and, when available, record reasons for lack of adherence or dropping out.**
- c. Develop graphical reports that dynamically show actual vs expected accrual. Develop programs to monitor for unexpected side effects and adverse events.**
- d. Check and clean data as they are collected.**

Interim Analyses of Data:

Interim analyses of data from the Menstrual Cycle Maintenance Study (Project 1) continued during the last year, leading to presentations, abstract, drafts of papers, and a DSMB report. These analyses have primarily examined:

- Description of the incidence of swelling over time for the first three years following surgery, what factors are associated with swelling, and how does swelling impact quality of life. This analysis was originally done during year 2 and has recently been updated using additional follow-up data.
- Description of menstrual bleeding patterns and factors associated with bleeding over time. The preliminary analysis of this data was originally done during year 2. During the last year, we updated the analysis using additional follow-up data focusing on the occurrence of bleeding rather than the patterns of bleeding. This analysis has led to a Biostatistics Seminar, a paper that is close to submission, and an abstract that will be submitted to ASCO next month. A second paper and abstract that will come from this analysis looks at the impact of early treatment related amenorrhea on subsequent bleeding. The analysis of patterns, which is a much more difficult analysis, will take place during the coming year. (See Appendix C.)
- Factors associated with quality of life during the first three years following the diagnosis of breast cancer. This analysis continued during the current year, resulting in a paper that is close to submission and an abstract that will be submitted to ASCO next month. (See Appendix C.)
- Factors associated with sexual arousal and satisfaction. A draft of a paper resulting from Marla McRae's master's thesis has been completed. One of the fellows, Dr. Stephanie Walsh, has also written a related paper on sexual function in women diagnosed with early stage breast cancer using data previously collected by Dr. Nancy Avis.
- An interim analysis of the RESTORE project was completed last year for a DSMB meeting. This analysis focused on accrual, missing data, adverse events, and the interim comparison of the two treatment arms with regard to quality of life and physical function.

The following analytic issues will continue to be addressed in the subsequent years of the grant as we focus more on data analysis:

- Missing and mistimed data (not all women enter the study at the same time in their disease course, not all women return forms each follow-up, not all women return every form for a particular follow-up, and not all women answer every question).
- How best to incorporate factors that lead to bleeding or lack of bleeding (e.g., pregnancies, some surgeries, etc.).
- How best to define/describe any period, regular periods, or cessation of periods.
- How best to handle left and interval censoring in analyzing time to certain events (e.g., time to first bleed, time to cessation of bleeding, etc.)

Tracking reports listing participant adherence and the receipt of participants' forms continue to be run weekly, so that participants can be contacted by coordinating center personnel if forms have not been received by their deadline dates. These reports are also used to assist the investigators and staff of Projects 1, 2 and 3 in devising retention strategies for study participants. For Project 3, we provide monthly graphical summaries of accrual.

Dropped participants reports including reasons were implemented for Projects 1, 2, and 3.

#### Quality Control Checks:

##### Menstrual Cycle Maintenance (Project 1):

We continue to perform quality control checks on the existing Menstrual Cycle Maintenance data. SAS programs were previously developed to check the validity of data within each form and to provide extensive error checking for chart reviews, demographic, medical history, medical history follow-up, symptoms, quality of life, and diary forms. This program continues to be updated as new forms (with new variables) are collected from participants.

##### Age Differences (Project 2):

Quality control features were built into the screens (e.g., range checks, field checks, skip patterns, etc.) to allow data validation at the point of data entry. Also, validation error reports were implemented, displaying outstanding errors for all forms, by Participant ID.

##### Restore (Project 3):

Quality control features are currently being programmed (e.g., range checks, field checks, skip patterns, etc.) to allow data validation at the point of data entry. Batch processing of errors will be implemented to check for errors in all the data that have been entered to date, prior to real-time error checking implementation. Validation error reports will be implemented, displaying outstanding errors for all forms, by Participant ID.

#### **Task 5: Analysis and Report (Months 41 – 48)**

- a. Convert the database to SAS and ASCII data sets for final analyses.**
- b. Help develop a publications and presentations policy.**
- c. Perform final data analyses and help prepare manuscripts and reports.**

These tasks will not take place until the last year of the grant. Currently the SQL database is converted to SAS regularly for quality control activities. Once all the data have been collected, edited, and corrected, a final SAS database will be created, including documentation for variable names and transformations. SAS transport and ASCII datasets will also be created to ensure maximum portability. These datasets will be stored on tape and on CDs (or the medium appropriate at that time).

### **PART III – KEY RESEARCH ACCOMPLISHMENTS**

- Enhancement of the web-based data management and tracking systems for each of the three projects and continued development of data entry facilities.
- Completed analysis of bleeding data for the Menstrual Cycle Maintenance Study (Project 1).
- Updated analysis of the swelling data for the Menstrual Cycle Maintenance Study (Project 1).
- Completed analysis of the sexual arousal and satisfaction data for the Menstrual Cycle Maintenance Study (Project 1).
- Ongoing analysis of quality of life data for the Menstrual Cycle Maintenance Study (Project 1).
- Completed interim analysis for the DSMB report for RESTORE (Project 3).

### **PART IV – REPORTABLE OUTCOMES**

#### **1) Presentations**

Menstrual Bleeding Following Surgery and Chemotherapy for Early Stage Breast Cancer – Doug Case, Biostatistics Seminar, April 2004.

2) Abstracts and papers using analyses performed in the Biostatistics Core are reported in the annual reports of each project.

### **PART V - CONCLUSIONS**

As in the previous year, the past year has been spent enhancing the infrastructure for the three projects in this award, including further development of data entry facilities, tracking systems,

and edit checks. Additionally, more focus has been placed on data analysis, and papers have been written on swelling, bleeding, sexual function, and quality of life. These should be published in the coming year. Patient accrual and follow-up is continuing for each project. During the next year, we should see the end of recruitment for Project 3 and an increased emphasis on the analysis of those data, while continuing the analysis of data collected in Project 1.

## **PART VI – REFERENCES**

N/A

**APPENDIX A:**  
**STUDY NEWSLETTERS TO PARTICIPANTS**



## Menstrual Cycle Maintenance and Quality of Life in Young Women with Breast Cancer Study

*Newsletter – May 2004*

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### Message from the Coordinating Center

#### Dear Study Participants:

Thank you so much for the cards and personal greetings you have sent us since the last newsletter. It is always good to hear about what is going on in your lives and to know that you appreciate the work we do. We all enjoy working on this study, primarily because of the contact we have with you.

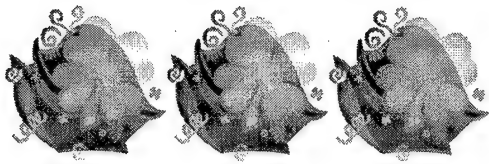
Registration to the *Menstrual Cycle Maintenance* study continues. We have enrolled 764 participants since January of 1998. Several of you are entering your seventh year of participating in this study. We appreciate the valuable information that we have received from all of you as you faithfully complete and return the questionnaires. We also appreciate your suggestions and comments, and the personal information that you share with us about your busy lives.

When the newsletters began in 1999, we ran a series of snapshot articles about the staff who work on the study. Since many of the newer participants may not know who we are, we thought now would be a good time to start this series again (**Staff Profile**). Included in this issue is an article about Debbie Allen, who is our administrative secretary for the Menstrual Cycle Maintenance Study. Among other responsibilities, Debbie completes all of the mailings to each of our study participants, and so she keeps very busy.

Also in this May 2004 issue, we are fortunate enough to have news from two participants (**Participant's Corner**). We enjoy hearing about the interesting things you are doing and so do other study participants. If you would like to share something with us for a future issue, (for example, inform us of a special support group, share your survivor story, recommend a good book or recipe, tell us about your hobbies or interests), please let us know – [ccorum@wfubmc.edu](mailto:ccorum@wfubmc.edu).

Continuing our commitment to giving the results of study analyses, this issue also features information about sexuality approximately 1 year after breast cancer surgery. We look forward to your comments.

## Incentive Winners



Here is an update on the winners since our last newsletter. (*Some winners chose not to have their names printed in the newsletter.*)

### CONGRATULATIONS to the following lucky winners!

For the fifteenth rewards drawing of gift cards, names were drawn in January 2004 from calendar and questionnaire entries:

**Donna Yenish-Kotchkowski**, Lyndhurst, NJ  
**Helen L. Bobryk**, West Hampton Beach, NY  
**Elizabeth O. Barrientos**, Westbrook, CT  
**Carol A. Hemenas**, Sugarland, TX  
**Marsalee W. Martin**, Trinity, NC  
**Rose M. Hill**, Brookline, MA  
**Aida Wellington**, Elmira, NY

For the sixteenth rewards drawing of gift cards, names were drawn in April 2004 from calendar and questionnaire entries:

**Eileen G. Cullen**, Brooklyn, NY  
**Beverly F. Slomka**, Brooklyn, NY  
**Beverly R. Woods**, Plymouth, IN  
**Carole J. Nix**, Winston-Salem, NC  
**Sharon L. Jenkins**, Friendswood, TX  
**Christina Delahunt-Bloom**, New York, NY

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Since our *Rewards Program* began in January 2000, we have had 113 winners. Winners receive a \$50 gift certificate from their choice of Home Depot, Lowe's Home Improvement, Walmart, or a Long Distance Calling Card.

For the newer participants, here's how it works:

- Your study materials (calendars and questionnaires) have an ID label on them which includes a due date. The due date indicates when the calendars and questionnaires need to be received at the Coordinating Center in order for you to be eligible for the quarterly drawings.
- Labels on the study materials received on or before their due date will be cut off and entered into the prize drawings.
- Seven winners are drawn quarterly. A participant can win the quarterly drawings only once.

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## Staff Profile

**Debbie  
Allen**



**Debbie Allen** has worked at Wake Forest University School of Medicine for five years. She lives in Winston-Salem, North Carolina with her husband, Benny. Debbie came to America from Angeles City, Panpanga in The Philippines in 1994, and became a US citizen in 2000. She plays the guitar, practices yoga, likes to read, and says she particularly enjoys picnicking on the Blue Ridge Parkway where she takes pleasure in the beauty of nature. She is also an active volunteer in community activities.

Debbie began working on the Menstrual Cycle Maintenance Study five years ago as secretary for Dr. Michelle Naughton, the



principal investigator for the study. Debbie's many responsibilities include making sure that each participant receives her mailings of calendars and/or questionnaires by the due date. Since we average about 200+ mailings a month, you can imagine that Debbie is an invaluable member of the coordinating center staff and one who keeps the study running smoothly.

### Websites



Fertile Hope is a national nonprofit organization dedicated to providing reproductive information, support and hope to cancer patients whose medical treatments present the risk of infertility. The organization was founded in 2001 by cancer survivor Lindsay Nohr as a result of her own endeavors to preserve her fertility in the face of critical cancer treatments. Fertile Hope is partnered with the Lance Armstrong Foundation to help meet the profound needs of patients whose medical treatments present the risk of infertility. Their website is: [www.fertilehope.org](http://www.fertilehope.org)

Information about the Department of Defense research program is at the following website: <http://cdmrp.army.mil>. Once you are on this website, click on the breast program, and scroll down the page to the Breast Cancer Research Program Fact Sheet: (<http://cdmrp.army.mil/pubs/factsheets/bcrpfactsheet.htm>), which includes a write-up on the history of the program.

## Participant Corner

### A Sailing Adventure

One of the study participants, Stacey Collins, is taking a 2-year sailing trip with her family and invites us to follow along by logging onto their website [www.sailnamaste.com](http://www.sailnamaste.com). Stacey says, "The trip was, of course, a response to my cancer experience. Gotta live for today!" We wish you the best, Stacey, and look forward to keeping up with your adventure.



### Tulips to Non-Profit: Watch Her Gardens Grow

by Patricia  
Mello

In June of 1998, I discovered on a baseline mammogram what turned out to be a benign fibroadenoma on my left breast. Three months later, I received the same diagnosis, but in the right breast. I felt very lucky and decided it was time to give back to the community, so I began volunteering for the Dallas Affiliate of Susan G. Komen Breast Cancer Foundation, and later became treasurer of the Dallas County Affiliate. I always felt that if I ever needed to rely on this wonderful group of people, they would be there for me. And sure enough, five years later, when I was 43 and diagnosed with breast cancer, my friends were there for me.

My first surgery was on April fool's day in 2003. I kept my sense of humor and joked with the doctors about it. Exactly one year

later, after a partial mastectomy, two surgeries, seven weeks of radiation and a "sentence" of Tamoxifen, I am doing great.

This past winter it was very important to me to have a renewal and celebration in the spring. I ordered over 200 bulbs from Holland and worked feverishly planting daffodil, tulip, hyacinth, and iris bulbs so they would come up on my first year anniversary. I was very thankful to have the energy to do this, and my garden this year produced incredibly vibrant pink, white, and yellow tulips and daffodils to help me celebrate life. It is wonderful to be able to share bouquets with my coworkers and family daily.

Almost weekly since July, I attend two different support groups: one at Richardson Regional Cancer Center in Richardson, Texas, and the other at The University of Texas Southwestern Medical Center in Dallas, Texas. Both groups have remarkably, courageous women in them who are a constant inspiration and support to me.

I have always been aware of how fortunate I am to still have a job and good health insurance. How many survivors do not have jobs and have to make hard choices about whether to pay for health insurance or the basics in life like food, rent, or mortgage payments? I, along with another survivor, were troubled by these questions and many more; and in a turning point in both of our lives and careers, decided to form a non-profit organization to help cancer survivors in the North Texas area. While we are both still employed full time, we work at night and on weekends to get this dream up and running. Our goal is, one year from now, to have funding to help our first group of survivors. Our long term plan after starting this in Texas is to take it nationwide. The most important thing a survivor should be concerned about is healing; she does not need the stress of financial obligations.

I have chosen to turn my breast cancer diagnosis into a positive experience. It has

helped me focus in on my purpose in life-- helping other survivors. This non-profit organization can help women with breast cancer by relieving some of their financial burden and thus allow them to concentrate on their care and wellness and leading a powerful life in the face of cancer.



### **We need you!**

We need you! Many of you have said that you are inspired by the personal survivor stories of other participants. If you are willing to share some interesting details about how you coped and thrived after your diagnosis, we would like to publish it here for other study participants to read.

---

### **Contact Information**

Carol S. Corum, Project Manager  
336-713-4268 or [ccorum@wfubmc.edu](mailto:ccorum@wfubmc.edu)

Doris Clark, Associate Project Manager  
1-888-278-1486 or [dclark@wfubmc.edu](mailto:dclark@wfubmc.edu)

Our address is:  
Wake Forest University Health Sciences  
Department of Public Health Sciences  
2000 W First St, PP II, 2<sup>nd</sup> Floor  
Winston-Salem, NC 27104

Fax (336) 716-7554  
Toll Free: 1-888-278-1486

## Sexual Functioning After Breast Cancer Treatment

Some younger women report changes in their sexual functioning after treatment for breast cancer. Part of these changes may be a result of the specific treatment they received and menstrual cycle variations, while other changes may be related to how women feel about themselves, their bodies, and their personal relationships after the end of treatment.

From the questionnaires that you have been completing over the past several years, we examined the factors related to greater sexual satisfaction and greater sexual arousal (or the ability to become physically aroused during sexual activity) at approximately 1 year after surgery for breast cancer.

Our analyses included 481 women who were approximately 9 – 15 months post surgery, and for whom we had complete medical chart review information regarding their cancer diagnosis and treatment. Of these 481 women, 387 participants indicated that they had been sexually active with a partner within the past month. Participants who had not been sexually active in the past month tended to have never married or were divorced/separated/widowed. They also tended to have a higher stage of cancer at diagnosis, to be of a slightly higher body weight, and to not be taking Tamoxifen or another hormone therapy after the end of active chemotherapy and/or radiation treatment. In addition, those women who were sexually inactive tended to report a lower overall quality of life, more depressive symptoms, and lower levels of social support in their daily lives.

Among those women who were sexually active, we examined three types of factors that might be related to their levels of sexual arousal approximately 1 year after breast cancer surgery. These factors were: demographic variables (including the woman's age, educational status, and race/ethnicity); clinical factors (type of surgery the woman had, type of treatment received, stage of disease at diagnosis, body mass index, change in body weight since diagnosis, current use of hormone therapy); and psychological and social factors (depressive symptoms, overall quality of life, sleep quality, social support, satisfaction with their appearance and body, their own avoidance of sexual activity, and their partner's avoidance of sexual activity). Only the following factors were found to be associated with *poorer* sexual arousal 9-15 months post-surgery for breast cancer:

- having had any form of chemotherapy as a treatment for breast cancer
- lower body mass index (a measure of weight in proportion to your height)

It is interesting to note that having a higher body mass index was associated with better sexual arousal. This result may be related to the fact that women with

higher body fat have greater levels of estrogen in their bodies, which may assist them in becoming physically aroused. It may also indicate health in these women, as they were able to gain or maintain a higher body weight post-treatment. None of the other factors examined were found to be significantly associated with a participants' sexual arousal, including the participants' age, race, type of surgery received (lumpectomy, mastectomy, reconstructive surgery), stage of disease, depressive symptoms, sleep quality, and the participants' satisfaction with their appearance.

Similar analyses were completed to examine breast cancer patients' levels of sexual satisfaction 9-15 months post-surgery. The types of factors examined were: demographic variables (including the woman's age, educational status, and race/ethnicity); clinical factors (type of surgery the woman had, type of treatment received, stage of disease at diagnosis, body mass index, change in body weight since diagnosis, current use of hormone therapy); and psychological and social factors (depressive symptoms, overall quality of life, sleep quality, social support, satisfaction with their appearance and body, their own avoidance of sexual activity, and their partner's avoidance of sexual activity). The following factors were found to be significantly associated with *greater* sexual satisfaction 9-15 months post-surgery:

- Having radiation therapy only (i.e., no chemotherapy)
- Women with higher satisfaction with their appearance and body
- Fewer depression-like symptoms
- Women not avoiding physical affection, particularly as it relates to their breasts or breast area

The type of surgery received (lumpectomy, mastectomy, reconstructive surgery); changes in body weight, body mass index, race or education were not found to be significantly associated with greater sexual satisfaction among the women in the study.

Thus, the examination of these topics indicate that for the women in this study, sexual arousal is more related to physiological factors, such as body weight and, potentially, estrogen levels and menopausal status. For sexual satisfaction, however, women's psychological state and feelings about their bodies have a greater impact on their levels of sexual satisfaction.



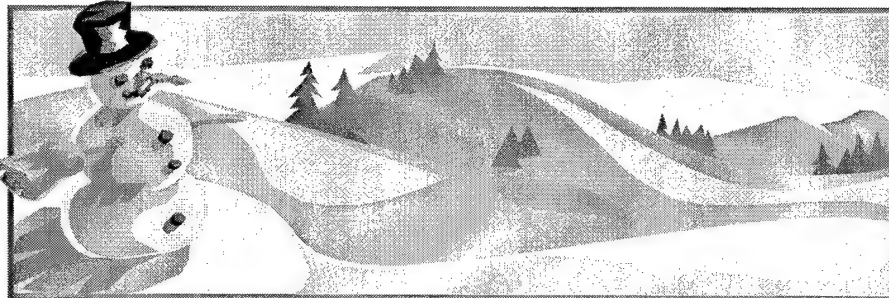
Menstrual Cycle Maintenance and Quality of Life  
in Young Women with Breast Cancer Study

**Newsletter – December 2003**

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**Wishing You a Beautiful Holiday Season  
and a New Year of  
Peace and Happiness**

From  
The Clinical Coordinating Center Staff at  
Wake Forest University School of Medicine  
and the Clinical Staffs of  
Memorial Sloan-Kettering Cancer Center  
M.D. Anderson Cancer Center  
Presbyterian Hospital of Dallas  
University of Texas Southwestern



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**Your Enclosure**

We have enclosed with this newsletter a booklet entitled *You Are Not Alone – A Guide and Resource Directory for Young Women with Breast Cancer*. This publication comes from a joint effort between the American Cancer Society and the Young Survival Coalition. Topics such as peer support, parenting while dealing with breast cancer, dealing with breast cancer as a single woman, and concerns about work and career are just a few of the issues that are addressed in an effort to let young women know they are not alone. We hope you find the booklet relevant and useful to your experience.



## Incentive Winners

Here is an update on the winners since our last newsletter. *(Some winners chose not to have their names printed in the newsletter.)*

### CONGRATULATIONS to the following lucky winners!

For the thirteenth rewards drawing of gift cards, names were drawn in July 2003 from calendar and questionnaire entries:

Farah Jaquith, Goshen, NY  
Ferne Pomerantz, Scarsdale, NY  
Rose Tervenski, Poughkeepsie, NY  
Jeanette Joyce, Arlington Heights, IL  
Monica Brabham, Dallas, TX  
Rhonda Perkins, Raleigh, NC

For the fourteenth rewards drawing of gift cards, names were drawn in October 2003 from calendar and questionnaire entries:

Diane Bradshaw, New York, NY  
Cecilia Romano, Staten Island, NY  
Denise Sortor, Colchester, VT  
Arlene Scavone, Islip, NY  
Courtney Coolidge, Houston, TX  
Sheila Ayers, Winston-Salem, NC

Since our *Rewards Program* began in January 2000, we have had 99 winners. Winners receive a \$50 gift certificate from their choice of Home Depot, Lowe's Home Improvement, Walmart, or a Long Distance Calling Card.

For the newer participants, here's how it works:

- Your study materials (calendars and questionnaires) have an ID label on them which

includes a due date. The due date indicates when the calendars and questionnaires need to be received at the Coordinating Center in order for you to be eligible for the quarterly drawings.

- Labels on the study materials received on or before their due date will be cut off and entered into the prize drawings.
- Seven winners are drawn quarterly. A participant can win the quarterly drawings only once.



## New Recipes

We have found a new website [www.copykat.com](http://www.copykat.com) on which recipes from famous restaurants are posted. We have chosen one that we hope you will enjoy during the holiday season.

### *Stanford Court Hotel Chestnut & Sausage Dressing*

*(from Stanford Court Hotel in San Francisco)*

#### Ingredients:

1 (1 lb.) loaf French Bread  
2 Tbsp. unsalted Butter  
1 yellow Onion, chopped  
1 Celery Stalk, chopped  
1/2 lb. well-seasoned fresh bulk Pork Sausage  
1/4 lb. ground Beef  
4 C. Milk  
1 (15 oz.) jar Prepared Fresh Chestnuts  
3 Tbsp. chopped Fresh Parsley  
Salt and Fresh Ground Pepper to taste  
1 tsp. chopped fresh Thyme

#### Preparation:

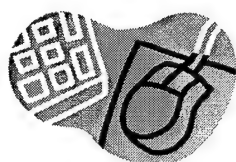
Tear bread into small chunks, spread out on a baking dish, and let dry overnight.



Preheat an oven to 375 degrees and butter a 9 x 13 inch baking dish. In a skillet over medium heat, melt the butter. Add the onion, and celery, and sauté, stirring occasionally, until translucent, 2 to 3 minutes; do not brown. Remove with a slotted spoon and reserve.

In the same pan, sauté the sausage and beef, stirring and mashing with a fork, until crumbled and cooked through, about 10 minutes. Drain off fat. Place the bread chunks in a large bowl and while tossing, gradually add the milk. Let stand, stirring occasionally, until the milk is absorbed and the bread is evenly moistened, 6 to 8 minutes.

Add the onion and celery, meat mixture, chestnuts and parsley. Season with salt and pepper, add the thyme, if desired, and mix well. Transfer dressing to baking dish and bake, until browned and crispy.



## Websites

Fertile Hope is a national nonprofit organization dedicated to providing reproductive information, support and hope to cancer patients whose medical treatments present the risk of infertility. The organization was founded in 2001 by cancer survivor Lindsay Nohr as a result of her own endeavors to preserve her fertility in the face of critical cancer treatments. Fertile Hope is partnered with the Lance Armstrong Foundation to help meet the profound needs of patients whose medical treatments present the risk of infertility. Their website is: [www.fertilehope.org](http://www.fertilehope.org)

The National Women's Health Information Center provides information on health-related topics of interest to women, their families, and friends. NWHIC's goals are to deliver fast, reliable and accessible health information to women everywhere. Their website is: [www.4woman.gov](http://www.4woman.gov)  
Toll Free number 1-800-994-WOMAN or  
TDD: 1-888-220-5446.

Information about the Department of Defense research program is at the following website: <http://cdmrp.army.mil>. Once you are on this website, click on the breast program, and scroll down the page to the Breast Cancer Research Program Fact Sheet: (<http://cdmrp.army.mil/pubs/factsheets/bcrpfactsheet.htm>), which includes a write-up on the history of the program.

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## Participant Corner

**We want to hear from you.** Many of you have said that you are inspired by the personal survivor stories of other participants. If you are willing to share some interesting details about how you coped and thrived after your diagnosis, we would like to publish it here for others study participants to read.

Our contact information is listed below. Please let us hear from you!



---

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## QUALITY OF LIFE AND DEPRESSIVE SYMPTOMS

The impact of breast cancer diagnosis and treatment can be quite marked for some women. In the first several years of the study, you completed a quality of life questionnaire for breast cancer patients, called the FACT-B, which was included in your questionnaire booklets. You also completed a depressive symptoms survey. The following provides information regarding the impact of breast cancer diagnosis and treatment on quality of life and depressive symptoms.

- **Health-Related Quality of life:**

Overall, participants' quality of life improved markedly at approximately 12-18 months diagnosis. Younger women reported lower levels of quality of life until 18-24 months post-diagnosis, at which time their quality of life became roughly the same as other age groups involved in the study. Women diagnosed at age 44 years or higher, had the highest levels of quality of life throughout the first 24 months after diagnosis. *(See Figure 1. Higher scores on the FACT-B indicated better overall quality of life.)*

Higher quality of life within the first 24 months post-diagnosis was associated with: being employed, having had no chemotherapy, being on tamoxifen or another type of hormone therapy, having a lower body mass index (BMI), consuming some alcohol, having high levels of social support, and having higher levels of spirituality.

Lower quality of life was associated with younger age at diagnosis, being non-white, and poorer sleep quality. Quality of life was the lowest for those participants who were diagnosed at age 30 or younger, although their quality of life was similar to patients of other age groups by 18-24 months post-diagnosis.

- **Depressive symptoms:**

Depressive symptoms decreased gradually over the follow-up period, particularly between 12 and 18 months post-diagnosis. *(See Figure 2. Lower scores indicate fewer depressive symptoms.)*

During the first year after diagnosis (months 1-12), higher depressive symptoms were noted for non-Hispanic white participants, those receiving any chemotherapy, those 35 years or younger at the time of diagnosis, lower social support, poorer sleep quality, and lower levels of spirituality.

During the second year after diagnosis (months 13-24), higher depressive symptoms were associated with being non-Hispanic white participants, being married/partnered, cigarette smoking, lower levels of social support, poorer sleep quality, and lower levels of spirituality. Younger age at diagnosis and chemotherapy were no longer found to be significant factors associated with depressive symptoms during the second year past diagnosis.



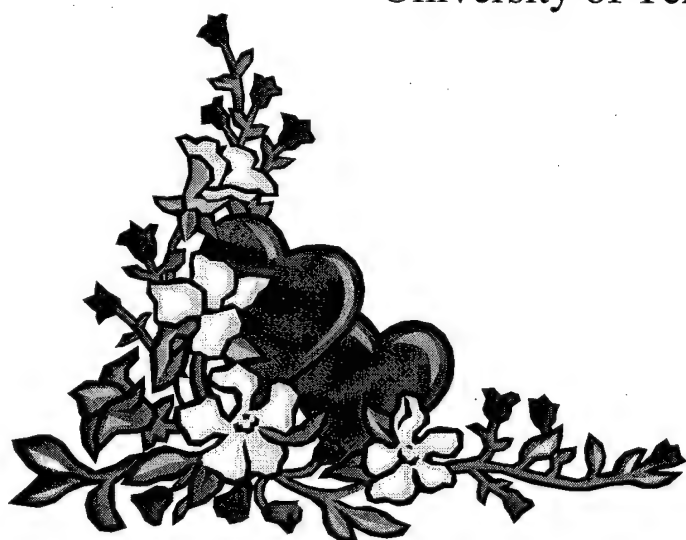
**APPENDIX B:**  
**VALENTINES DAY LETTER**

# HAPPY VALENTINE'S DAY!

We appreciate your  
valuable participation in the  
Menstrual Cycle Maintenance Study

The Clinical Coordinating Center Staff at  
Wake Forest University Health Sciences  
and

The Clinical Staffs of  
Memorial Sloan-Kettering Cancer Center  
M.D. Anderson Cancer Center  
Presbyterian Hospital of Dallas  
University of Texas Southwestern



**APPENDIX C:**  
**ANALYSES OF MENSTRUAL CYCLE MAINTENANCE DATA**

## **Menstrual Cycle Maintenance and Quality of Life After Breast Cancer Treatment**

Michelle Naughton, Ph.D., Jeanne Petrek, M.D.,  
L. Douglas Case, Ph.D., Sally Shumaker, Ph.D.,  
Electra Paskett, Ph.D., Elizabeth Naftalis, M.D.

## **Background**

- 15% of annual invasive breast cancers will occur in women of childbearing age.
- Greater than 80% will be long-term survivors.
- Most patients will have chemotherapy.
- At least 50% will suffer ovarian failure, resulting in premature menopause and other health effects.

## **Quality of Life Concerns**

- Younger women are at a different "life stage" than post-menopausal women.
- Psychological responses: anxiety, depression
- Impact of premature menopause on daily life
- Fertility and pregnancy concerns

## **Gaps in Knowledge**

- The incidence, onset, time course, and symptoms associated with premature menopause are largely unknown.
- Impact of premature menopause on the young survivor's quality of life over time has not been studied.

## **Symptoms**

- Menopausal symptoms:
  - hot flushes
  - sleep disturbance
  - decreased libido
  - vaginal dryness

## **Factors Associated with TRA**

- Patient Age
- Type of treatment (e.g., chemotherapy vs. radiation)
- Category of chemotherapy drug used:
  - Alkylating agents (e.g., cyclophosphamide)
  - Doxorubicin
  - Taxol, taxotere
  - Tamoxifen?

### **Limitations of Previous Studies**

- Retrospective studies
- Varying definitions of temporary or permanent amenorrhea
- Variable lengths of follow-up on menses
- Secondary endpoint in analyses of cancer treatment.

### **Fertility and Pregnancy: Questions**

- Who are those women who maintain their fertility after systemic therapy?
- Incidence of subsequent pregnancy and successful childbearing is unknown.
- Self-selection of women with less aggressive tumors who become pregnant.
- Does pregnancy provide a tumor suppressing effect.

### **Study Objectives**

- To describe the menstrual bleeding patterns of female breast cancer patients aged 45 years or younger after treatment.
- To compare the incidence of treatment - related amenorrhea (TRA) by mode of treatment and patient characteristics.

### **Study Objectives**

- To describe the quality of life of young women with breast cancer at 6 month intervals from the time of recruitment.
- To create a cohort of patients from which to track subsequent pregnancies and their effect on patients' (and their infants') morbidity and mortality.

### **Eligibility Criteria**

- Female
- Age 18-45 at diagnosis
- Be diagnosed with a first breast cancer, stage I, II, or III, with the previous six months
- Receiving treatment for the condition
- Still having regular menstrual cycles at the time of diagnosis.

### **Participating Centers**

- Memorial Sloan-Kettering Cancer Center, New York City
- Wake Forest University Medical Center, Winston-Salem, North Carolina
- M.D. Anderson Cancer Center, Houston, Texas
- Presbyterian Hospital, Dallas, Texas
- Univ. of Texas-Southwestern, Dallas, Texas

### Study Requirements

- Complete study questionnaires every 6 - 12 months:
  - Medical and reproductive history
  - current medications
  - symptoms
  - health-related quality of life forms
  - arm and hand swelling questions

### Study Requirements

- Monthly menstrual bleeding calendars:
  - frequency, duration, and amount of monthly bleeding

### Clinical Data

- Chart Review Data:
  - tumor pathology
  - surgery
  - treatment(s)
  - recurrences
  - new site diagnosis
  - co-morbidities

### Recruitment

- Recruitment began at 4 clinical centers in January of 1998.
- Recruitment is still on-going at 2 centers until December 31, 2005.
- To date, 734 women have been recruited to the protocol. We will recruit 100 more participants.
- Follow-up is continuing for 70% of the cohort.

### Study Results

- Based on 628 participants who were recruited between January 1, 1998 – July of 2002.
- Results will be presented for:
  - Menstrual bleeding following treatment
  - Quality of life effects following diagnosis and treatment
  - Sexual functioning 1 year post-surgery

Summary of Participant Characteristics

Characteristic	# (%)
<b>Clinic</b>	
Sloan-Kettering	426 (72)
MD Anderson	86 (14)
Wake Forest	47 (8)
Presbyterian	36 (6)
Median Age in Years (Range)	39.5 (20 – 45)
<b>Age at Diagnosis in Years</b>	
[20 – 24)	2 (<1)
[25 – 29)	36 (6)
[30 – 34)	108 (18)
[35 – 39)	174 (29)
≥ 40	275 (46)
Median BMI in kg/m <sup>2</sup> (Range)	23.2 (16.9 – 56.9)
<b>Race/Ethnicity</b>	
Caucasian	526 (88)
African-American	28 (5)
Hispanic	25 (4)
Asian/Pacific Islander	16 (3)

**Summary of Participant Characteristics**

Characteristic	# (%)
<u>Marital Status</u>	
Single/Separated/Widowed	146 (25)
Married/Marriage-like	449 (75)
<u>Education</u>	
< 4 year College Graduate	204 (34)
4 yr College Graduate/Graduate School	390 (66)
<u>Employment</u>	
Unemployed/Looking	16 ( 3)
Full-time Homemaker	101 (17)
Full-time	325 (55)
Part-time	85 (14)
Disabled	37 ( 6)
Other	30 ( 5)

**Summary of Participant Characteristics**

Characteristic	# (%)
<u>Income</u>	
< 50K/Year	168 (29)
50-100K/Year	222 (38)
> 100K/Year	194 (33)
<u>Smoke 100 Cigarettes</u>	
No	338 (57)
Yes, Former Smoker	215 (36)
Yes, Current Smoker	42 ( 7)
<u>Age at First Menstrual Period</u>	
≤ 10	36 ( 6)
11	98 (16)
12	180 (30)
13	174 (29)
14	63 (11)
≥ 15	44 ( 7)
<u>Full Term Births</u>	
0	222 (37)
1	115 (19)
2	177 (30)
3	64 (11)
4+	17 ( 3)

**Summary of Local Treatment and Tumor Characteristics**

Characteristic	# (%)
<u>Breast Surgery</u>	
Lumpectomy	306 (51)
Mastectomy with Radiation Therapy	122 (21)
Mastectomy without Radiation Therapy	167 (28)
<u>Tumor Size (cm)</u>	
≤ 2 cm	372 (65)
2 - 5 cm	169 (30)
> 5 cm	28 ( 5)
<u>Nodal Dissection</u>	
None	9 ( 2)
Sentinel Only	26 ( 4)
Axillary Dissection	355 (60)
Sentinel and Axillary Dissection	201 (34)

**Summary of Local Treatment and Tumor Characteristics**

Characteristic	# (%)
<u>Nodes Examined</u>	
0	10 ( 2)
1 - 10	193 (33)
11 - 20	247 (42)
> 20	144 (24)
<u>Nodes Positive</u>	
0	334 (56)
1-3	163 (27)
4-9	58 (10)
10+	40 ( 7)

## Family History

- Of those with a family history:
  - 23% had 1 female relative with a prior breast cancer
  - 5% had 2 female relatives
  - 1% had 3 female relatives

## Other Factors

- Average age of onset of menses: 12.5 years (22% began before 12 years of age)
- Average age of first pregnancy 27.6 years
- 39% had their first pregnancy at age 30 or above
- 35% were regular smokers at diagnosis (avg. # years smoking = 9.7; range 3-15).

## Menstrual Bleeding Patterns

## Menstrual Bleeding

### Principal Investigators:

- Dr. Jeanne Petrek, Memorial Sloan Kettering Cancer Center, New York
- Senior Statistician: Dr. Doug Case
- Dr. Michelle Naughton

### Major Objectives:

- How does treatment effect menstrual bleeding?
- What are the characteristics of those who maintain menstrual cycles?

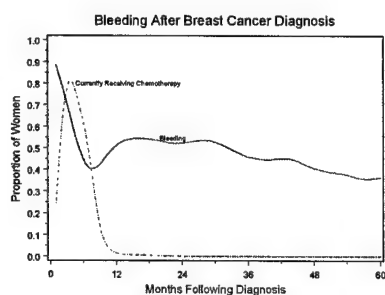


Figure 1. Monthly bleeding following the diagnosis of breast cancer (solid line) and the proportion of women receiving chemotherapy (dotted line).

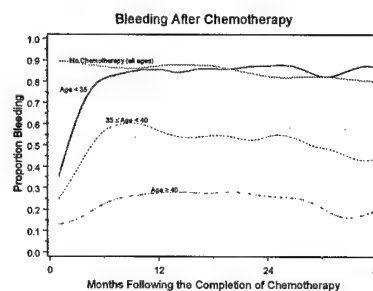


Figure 2. Proportion of women with monthly bleeding from time of completion of their chemotherapy program. The age year noted is age at diagnosis.

Mean Proportion of Women with Monthly Bleeding by Year Following the End of Chemotherapy

	1 <sup>st</sup> Year			2 <sup>nd</sup> Year			3 <sup>rd</sup> Year		
	N	Mean	SD	N	Mean	SD	N	Mean	SD
<b>Total</b>	500	.43	.38	409	.49	.42	331	.44	.43
<b>Age Group</b>									
< 35	126	.72	.31	94	.86	.25	66	.87	.28
35 – 39	156	.50	.36	122	.55	.39	98	.54	.40
≥ 40	218	.21	.29	193	.28	.36	167	.22	.33
<b>Chemotherapy Regimen</b>									
AC	118	.53	.38	103	.59	.40	84	.59	.40
ACT	155	.39	.37	123	.50	.42	95	.43	.43
CMF	82	.44	.39	67	.30	.35	61	.25	.36

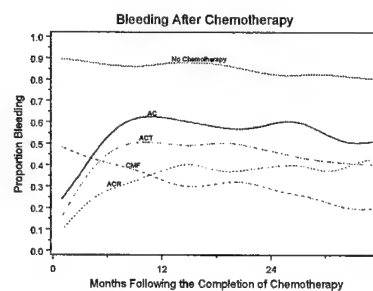
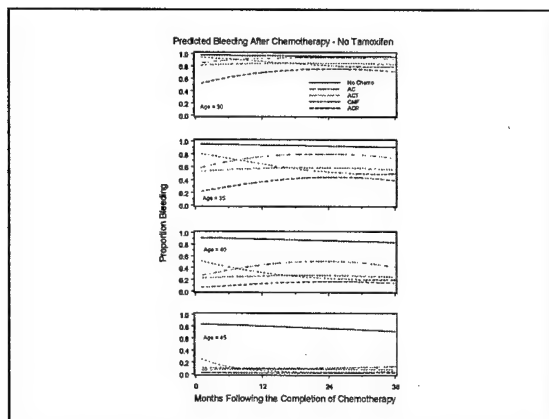


Figure 3. Proportion of women with monthly bleeding starting from time of completion of their specific chemotherapy program.





**Results from Logistic Regression Model Assessing Effects of Covariates on Bleeding**

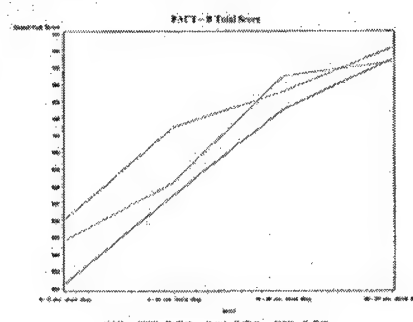
Characteristic	OR (95% CI)
<b>Women With Chemotherapy</b>	
Age	.76 (.74 - .79)
Nodes Positive	.89 (.84 - .94)
<b>Months After Chemotherapy</b>	
	1 Month 12 Months 24 Months 36 Months
Tamoxifen *	1.23 (.95 - 1.60) .50 (.37 - .67) .43 (.28 - .61) .80 (.50 - 1.29)
Chemotherapy *	1.54 (0.94 - 2.53) 1.13 (0.73 - 1.75) 1.13 (0.68 - 1.89) 1.61 (0.85 - 3.04)
<b>Women Without Chemotherapy</b>	
Age	0.87 (0.75 - 1.02)
Education	3.55 (1.73 - 7.30)
Full-term Births	1.59 (1.07 - 2.38)
Time (Months)	0.98 (0.96 - 1.00)

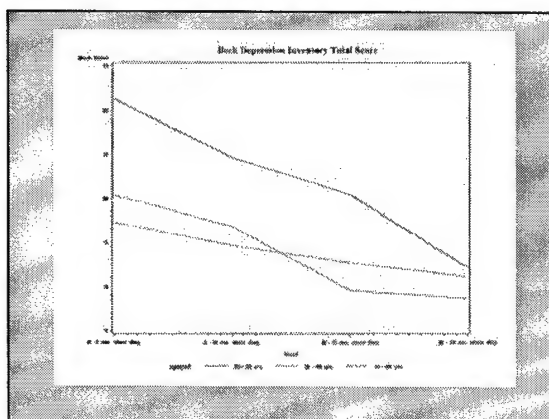
## Menopausal Symptoms

## Menopausal Symptoms

	Months		
	6	12	18
• Restless Sleep:	79	68	68
• Low Energy:	80	80	77
• Feeling Depressed:	67	59	54
• Mood Changes:	66	64	63
• Vaginal Dryness:	40	41	43
• Night Sweats:	37	45	46
• Hot Flashes:	36	55	56

## Quality of Life





Premenopausal Breast Cancer Patients HRQL Since Diagnosis (By Year)			
	FACT Total 1 Year	FACT Total 1-2 Years	FACT Total 1-3 Years
<b>Demographic Variables:</b>			
Age	0.1892	0.2124	0.1828
Race	0.2558	0.0008	0.0028
Education	0.2958	0.2958	0.0396
Marital Status	0.7439	0.4339	0.5875
Number of Children	0.6885	0.1001	0.1517
<b>Clinical Variables:</b>			
Stage at Diagnosis	0.6789	0.6815	0.5744
Chemotherapy	0.2555	0.0183	0.0207
Mastectomy w/ Radiation	0.2575	0.1192	0.2008
Mastectomy w/o Radiation	0.4328	0.5433	0.6393
Reconstructive Surgery	0.2881	0.7213	0.9603
Satisfaction w/ Appearance	<.0001	<.0001	<.0001
Time since diagnosis	0.0059	0.0009	<.0001
% Bleeding days (last 3 mos)	0.2200	0.0503	0.1191
<b>Lifestyle Variables:</b>			
BMI	0.4046	0.3630	0.4259
Smoking Per Day	0.1422	0.2035	0.2045
Alcohol Per Month	0.2248	0.1559	0.2787
Moderate Weekly Exercise	0.6360	0.0121	0.0008
Social Support	<.0001	<.0001	<.0001

## Sexual Functioning

## Sexual Functioning

- Marla MacRae, M.S.
- Doug Case, Ph.D.
- Michelle Naughton, Ph.D.
- Research Question:
  - What is the sexual functioning of patients approximately 1 year post-surgery in relation to sexual arousal and sexual satisfaction?

Table 1. Demographic Characteristics of Participants by Self-Reported Sexual Activity

	Sexually Active # ( % )	Sexually Inactive # ( % )	p-value
Total	401 (100)	84 (100)	
<b>Race/Ethnicity</b>			.99
White (non Hispanic)	360 (90)	75 (89)	
Black/African-American	14 (3)	3 (4)	
Hispanic	16 (4)	4 (5)	
Asian/American Indian	11 (3)	2 (2)	
<b>Age</b>			.05
Mean (SD)	39.6 (5.0)	40.7 (4.1)	
Median (Range)	40.7 (21-47)	42.2 (26-47)	
<b>BMI</b>			.05
Mean (SD)	24.5 (4.9)	25.7 (5.6)	
Median (Range)	23.3 (17.0-48.2)	24.6 (17.7-43.2)	

Table 1 (cont.). Demographic Characteristics of Participants by Self-Reported Sexual Activity

	Sexually Active # ( % )	Sexually Inactive # ( % )	p-value
<b>Marital Status</b>			<.0001
Never Married	34 ( 8 )	42 (50)	
Presently Married	318 (79)	28 (33)	
Marriage-like relationship	20 ( 5 )	2 ( 2 )	
Divorced/Separated/Widowed	29 ( 7 )	12 (14)	
<b>Education</b>			.64
Less than High School Grad.	4 ( 1 )	0 ( 0 )	
High School Degree	29 ( 7 )	5 ( 6 )	
Business/Vocational School	17 ( 4 )	4 ( 5 )	
Some College (no degree)	59 (15)	13 (15)	
Associate Degree	30 ( 7 )	6 ( 7 )	
College Graduate	117 (29)	17 (20)	
College/Prof. School Post Grad.	35 ( 9 )	10 (12)	
Master's Degree	85 (21)	20 (24)	
Doctoral Degree	25 ( 6 )	9 (11)	

**Table 2. Clinical Characteristics of Participants by Self-Reported Sexual Activity \***

Characteristics	Sexually Active # ( % )	Sexually Inactive # ( % )	p-value
Total	401 (100)	84 (100)	
<u>Months post surgery</u>			.55
Mean (SD)	12.2 (1.6)	12.1 (1.5)	
Median (Range)	12.5 (9.1 - 15)	12.1 (9.1 - 14.8)	
<u>Tumor Size</u>			.03
≤ 2 cm	252 (67)	44 (55)	
2 - 5 cm	108 (29)	28 (35)	
> 5 cm	15 (4)	8 (10)	
<u>Nodes Positive</u>			.21
0	224 (56)	48 (57)	
1-3	113 (28)	19 (23)	
4-9	40 (10)	7 (8)	
10+	24 (6)	10 (12)	

**Table 5. Multivariable Regression Models for Sexual Arousal and Satisfaction: Demographic and Clinical Factors**

Variable	Arousal		Satisfaction	
	$\beta$	p-value	$\beta$	p-value
Age	-0.0323	.48	0.0317	.27
Race (W vs B)	0.0502	.94	0.1069	.80
Education (≥ College vs < College)	0.1580	.72	-0.1888	.50
<u>Primary Treatment</u>		.06		.30
Mastectomy w/o RT vs Lumpectomy	-0.7554		-0.0704	
Mastectomy with RT vs Lumpectomy	1.0256		0.6850	
<u>Nodes Positive</u>		.67		.73
1-3 vs 0	0.1451		-0.1524	
4+ vs 0	-0.5268		0.1982	
<u>Tumor Size</u>		.10		.34
2-5 cm vs ≤ 2 cm	-0.9509		-0.4560	
> 5 cm vs ≤ 2 cm	0.4671		-0.1206	
Chemotherapy	-0.8493	.23	-0.2574	.57
Hormone Therapy	0.1931	.65	0.4539	.10
Time Since Surgery (Months)	-0.1433	.25	-0.0336	.67
Menstrual Bleeding	2.1276	<.0001	1.1367	.0004
BMI	0.1253	.01	-0.0104	.72
Change in Weight (lbs)	-0.0097	.57	-0.0133	.22

**Table 2 (cont.). Clinical Characteristics of Participants by Self-Reported Sexual Activity\***

Characteristics	Sexually Active # ( % )	Sexually Inactive # ( % )	p-value
<u>Primary Treatment</u>			.48
Lumpectomy	210 (52)	38 (4)	
Mastectomy without RT	112 (28)	26 (31)	
Mastectomy with RT	79 (20)	20 (24)	
Immediate Reconstruction	127 (32)	20 (24)	.15
Chemotherapy	352 (88)	73 (87)	.82
Hormone Therapy	244 (61)	43 (51)	.10
Menstrual Bleeding**	247 (64)	42 (52)	.05
<u>Change in Weight</u>			.75
Mean (SD)	3.5 (12.1)	4.0 (14.7)	
Median (Range)	2.0 (-32, 119)	4.0 (-60, 55)	

\* Not all participants answered every question  
\*\* Any bleeding in previous 90 days

**Table 6. Full and Reduced Regression Models for Sexual Arousal**

Variable	Full Model		Reduced Model	
	$\beta$	p-value	$\beta$	p-value
<u>Demographic</u>				
Age	-0.0605	.18		
Race (W vs B)	-0.2235	.73		
Education (≥ College vs < College)	-0.0533	.90		
<u>Clinical</u>				
<u>Primary Treatment</u>		.11		
Mastectomy w/o RT vs Lumpectomy	-0.5964			
Mastectomy with RT vs Lumpectomy	0.9514			
<u>Nodes Positive</u>		.56		
1-3 vs 0	0.1362			
4+ vs 0	-0.6456			
<u>Tumor Size</u>		.08		
(2-5) vs ≤ 2	-0.9958			
> 5 vs ≤ 2	0.3739			

**Table 3. Mean Scores and Standard Deviations of Quality of Life Measurements**

Instrument (range)	Cronbach's Alpha	Sexually Active	Sexually Inactive	p-value
Total Sample Size		401	84	
WHIRS Sleep Quality (0-25)	0.85	10.2 (5.7)	10.7 (5.2)	.53
Fact-B Total Score (0-148)	0.89	115.3 (17.2)	106.8 (20.5)	<.0001
Total Beck Depression (0-63)	0.85	8.1 (6.2)	10.0 (7.4)	.02
Satisfaction with Appearance (8-40)	0.86	26.7 (7.0)	25.6 (6.7)	.17
MOS Total Social Support (0-100)	0.97	82.0 (18.1)	66.1 (22.3)	<.0001

**Table 6 (cont.). Full and Reduced Regression Models for Sexual Arousal**

Variable	Full Model		Reduced Model	
	$\beta$	p-value	$\beta$	p-value
Chemotherapy	-0.6658	.33		
Hormone Therapy	-0.2608	.54		
Time Since Surgery (Months)	-0.1359	.26		
Menstrual Bleeding	1.4765	.003	1.8836	<.0001
BMI	0.1521	.001	0.1410	.001
Change in Weight (lbs)	-0.0004	.98		
<u>Psychosocial</u>				
Depression	-0.0713	.09		
Sleep Quality	-0.0688	.07	-0.1034	.003
Social Support	-0.0104	.41		
Appearance	0.0579	.10	0.0764	.01
<u>Physical Affection</u>				
I avoid it	-0.2180	.06	-0.2352	.01
My partner avoids it	-0.1081	.40		

**Table 7. Full and Reduced Regression Models for Sexual Satisfaction**

Variable	Full Model		Reduced Model	
	$\beta$	p-value	$\beta$	p-value
<b>Demographic</b>				
Age	0.0063	.81		
Race (W vs B)	-0.1530	.68		
Education ( $\geq$ College vs < College)	-0.3062	.21		
<b>Clinical</b>				
Primary Treatment				
Mastectomy w/o RT vs Lumpectomy	-0.2127	.16		
Mastectomy with RT vs Lumpectomy	0.7844			
Nodes Positive				
1-3 vs 0	-0.2254	.53		
4+ vs 0	0.1758			
Tumor Size				
(2-5) vs $\leq 2$	-0.5321	.12		
> 5 vs $\leq 2$	0.1283			

## Summary

- Quality of life is improving over time. Biggest gains occur approximately 12-18 months post diagnosis and treatment.
- Young women in the cohort report a reduced quality of life as compared to the women aged 40 years or older.

**Table 7 (cont.). Full and Reduced Regression Models for Sexual Satisfaction**

Variable	Full Model		Reduced Model	
	$\beta$	p-value	$\beta$	p-value
Chemotherapy	-0.1600	.68		
Hormone Therapy	-0.0102	.97		
Time Since Surgery (Months)	-0.1033	.85		
Menstrual Bleeding	0.5161	.07	0.5582	.01
BMI	0.1023	.64		
Change in Weight (lbs)	-0.0081	.41		
<b>Psychosocial</b>				
Depression	-0.0898	.0002	-0.0979	<.0001
Sleep Quality	-0.0302	.17		
Social Support	-0.0016	.83		
Appearance	0.0284	.16	0.0414	.02
<b>Physical Affection</b>				
I avoid it	-0.1421	.03	-0.1423	.022
My partner avoids it	-0.2474	.001	-0.2122	

## Summary

- Sexual arousal 1 year post-surgery appears to be, in part, related to physical factors (i.e., bleeding status, BMI).
- Sexual satisfaction 1 year post-surgery is more influenced by psychosocial factors such as depressive symptoms, satisfaction with appearance, and avoidance of sexual activities.

## Summary

- Proportion of women who bleed following treatment will vary by their age and particular chemotherapy regimen received.
- Menopausal symptoms increased during the first year after treatment and are continuing, particularly hot flashes and night sweats.

**APPENDIX D:**  
**PROJECT 3 (RESTORE): INCENTIVE PROGRAM**

## Appendix D: RESTORE Exercise & Control Group Current Incentives Program Proposal

Control Group	Intervention Group
<p><b>Gift At Randomization</b></p> <p>Participants are given face-to-face notification of group assignment upon randomization at the Baseline 1 visit.</p> <p>Gifts:</p> <ul style="list-style-type: none"> <li>• \$25 gift certificate of choice</li> </ul> <p><b>Cost: \$1250</b></p>	<p><b>Gift At Randomization</b></p> <p>No gift, but participants are given face-to-face notification of group assignment.</p>
<p><b>Testing Visit Rewards Program</b></p> <p>Participant will earn a dollar amount following successful completion of each testing visit based on the schedule below.</p> <p>Baseline-0 = \$15 Baseline-2 = \$10 OR BC Visit = \$25</p> <p>6-mo = \$5 9-mo = \$5 15-mo = \$5 18-mo = \$10</p> <p><b>Cost: \$ 2500</b></p> <p>Reward will be the accrued dollar amount in the form of a gift certificate of choice. Note: Existing participants phasing into program will begin accruing points at their next scheduled testing visit. Study dropouts receive gift certificate based on the number of points accrued during period of participation.</p>	<p><b>Testing Visit Rewards Program</b></p> <p>Participant will earn a dollar amount following successful completion of each testing visit based on the schedule below.</p> <p>Baseline-0 = \$15 Baseline-2 = \$10 OR BC Visit = \$25</p> <p>6-mo = \$5 9-mo = \$5 15-mo = \$5 18-mo = \$10</p> <p><b>Cost: \$ 2500</b></p> <p>Reward will be the accrued dollar amount in the form of a gift certificate of choice. Note: Existing participants phasing into program will begin accruing points at their next scheduled testing visit. Study dropouts receive gift certificate based on the number of points accrued during period of participation.</p>
<p><b>Individual Feedback Session</b> Add 9-month Session</p>	<p><b>Individual Feedback Session</b> Already provided</p>

#### **Ongoing Incentive Gifts Program for Both Groups**

- Baseline: T-shirt and Pedometer
- 3-Mo: First gift certificate accrued from baseline given at first testing feedback session for controls and at the exercise orientation session for exercise group members.
- 6-Mo: Water bottle
- 9-Mo: Feedback session
- 15-Mo: Note pad
- 18-Mo: Final feedback session + Final gift certificate

#### **Program Implementation Process**

- Program to begin for all new participants in 8/04. Starting on that date, testing visit rewards will be retroactive for all active participants in the exercise group based on number of visits successfully completed.
- All new participants will receive face-to-face incentives program orientation at randomization.
- Testing visit rewards system tracked by coordinating staff.
- New incentives program will be announced to control group members in the July newsletter and by letter mailed to existing active participants in August. Announcement will include discontinuation of bimonthly lecture series, but maintenance of bimonthly newsletters and addition of 9-month individual feedback session. Active exercise group members will be notified of incentives plan by August letter as well.